DIABETIC FOOT ULCER AND MULTIDRUG - RESISTANT ORGANISMS: PREVALENCE AND RISK FACTORS

A HOSPITAL BASED CROSS-SECTIONAL STUDY

Dissertation submitted to

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI

In partial fulfillment of the degree of

M.S. GENERAL SURGERY

Branch- I

PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH, COIMBATORE

DEPARTMENT OF GENERAL SURGERY

APRIL 2013

CERTIFICATE

This is to certify that **DR.K.MANIKANDAN** postgraduate student (2010-2013) in the department of General Surgery, PSG INSTITUTE OF MEDICAL SCIENCES AND RESEARCH, Coimbatore has done this dissertation titled **" DIABETIC FOOT ULCER AND MULTIDRUG – RESISTANT ORGANISMS : PREVALENCE AND RISK FACTORS - A HOSPITAL BASED CROSS-SECTIONAL STUDY "** under the direct guidance and supervision of guide Prof .DR.VIMAL KUMAR GOVINDAN and co-guide Prof .DR.JAYALAKSHMI in partial fulfillment of the regulations laid down by the **Tamilnadu Dr.M.G.R. Medical university**, Chennai, for M.S., Branch – I General Surgery degree examination.

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DECLARATION

I, **Dr. K.MANIKANDAN**, solemnly declare that this dissertation **" DIABETIC FOOT ULCER AND MULTIDRUG – RESISTANT ORGANISMS : PREVALENCE AND RISK FACTORS - A HOSPITAL BASED CROSS-SECTIONAL STUDY "** is a bonafide record of work done by me in the Department of General Surgery, PSG Institute of Medical Sciences and Research, Coimbatore, under the guidance of **Prof. DR. VIMAL KUMAR GOVINDAN, M.S, FRCS.**

This dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the University regulations for the award of MS Degree (General Surgery) Branch-I, Examination to be held in April 2013.

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ACKNOWLEDGEMENT

I wish to thank PSG HOSPITALS for having permitted me to conduct this study in this hospital.

I am ever grateful to all the faculty members of Department of General Surgery and Microbiology, PSG IMS&R for their generous help, kind guidance, valuable advice, expert supervision & encouragement throughout my career & for the preparation for this dissertation.

Last but not the least, I express my gratitude to all the patients for their cooperation for being a part of my study, my colleagues, parents and wife for their support and blessings, without whom nothing would have been possible in this world.

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INTRODUCTION

Diabetes mellitus is a chronic disease with chronic microvascular and macrovascular complications. India is considered by many, as the diabetic capital of the world. Like in other developing countries, complications of diabetic foot such as ulceration and infections, apart from causing high morbidity and mortality, also have social, and economic ramifications (Ako et al., 2006[10]; Shankar et al., 2005[11]; Gadepalle et al., 2006[12]). It has been reported that as high as 15 % of all diabetics are prone to develop ulcers in their feet during their life time. These can result in severe tissue destruction and can lead to some form of amputation (Lipsky et al., 2004[13]). The major concern at present is the increasing incidence of multi-drug resistant organisms. The problem of multi-drug resistant organisms were poorly studied because of lack of uniform definitions and specific criteria to name an organism as multi-drug resistant. The European center for disease control and prevention has defined criteriae, which are applicable universally. Very few studies have been done in India to analyse the prevalence and risk factors of multi-drug resistant organisms in relation to diabetic foot ulcers. The impact caused by multi-drug resistant organism were least analysed in Indian litearature. Hence this study was done to analyse the prevalene, riskfactors and impact of multi-drug resistant organisms in diabetic foot ulcers at a tertiary care hospital.

ABSTRACT

Aim:

To study the prevalence, risk factors and impact of multi-drug resistant organism (MDRO) infection in diabetic foot ulcers.

Methodology:

150 diabetic patients with foot ulcer were prospectively studied. Detailed clinical history and clinical examination of the ulcer were done for all patients. Patients were screened for neuropathy, nephropathy, retinopathy, peripheral arterial disease and underlying osteomyelitis using appropriate methods. The microbiological profile was analyzed in detail for each patient. Using internationally accepted criteria, the multidrug resistant organisms were identified.

Infected ulcers were grouped into those with MDRO and those without MDRO and were then compared using univariate analysis. In order to identify the risk factor, for the presence of MDRO, analysis by logistic regression was done. Each patient was followed for a period of ten weeks to assess the status of wound healing. The impact of MDRO was assessed by analyzing the associations of amputations, duration of hospital stay, status of wound at ten weeks with MDRO infected ulcers using appropriate statistical tools. The influence of other factors on wound healing were analyzed by the same statistical tools.

Results :

MDRO were isolated from 99 patients of 150 (66 %). 54.8 % (153 out of 279) of isolated organisms were multidrug resistant organisms. The commonest organism isolated in our study was Escherechia coli followed by Staphylococcus aureus and Pseudomonas aeruginosa. By univariate analysis poor glycaemic control, previous hospitalisation, previous history of amputation, previous antibiotic usage, size of ulcer, necrotic ulcer, recurrent ulcers, higher grade of ulcer, presence of osteomyelitis, presence of retinopathy, peripheral vascular disease, neuropathy and polymicrobial culture, were associated with significance in those with MDRO infected foot ulcers.

Analysis by Logistic regression indicated that, only two factors significantly increased the risk of acquiring MDRO infection; 1) recurrent ulcer (OR = 3.39, $p < 0.05$, 95 % CI = [1.081 – 10.664]), 2) Higher grade of ulcer (OR = 13.44, $p < 0.001$, 95 % CI = [3.595 – 50.278]). It was found that the mean duration of hospital stay of patients with MDRO infections was 15.36 days ($p < 0.001$). MDRO in the foot ulcers significantly increased the frequency of amputations ($p < 0.01$).

MDRO infected ulcers had no impact on wound healing although they were significant by univariate analysis. By Logistic regression, age (OR = 0.942, $p <0.1$, 95 % CI = [0.882 – 1.005]), presence of PVD (OR = 7.872, $p < 0.01$, 95 % CI = [2.009 – 30.849]), osteomyelitis (OR = 8.280, $p<0.01$, 95 % CI = [1.768 – 38.766]), nephropathy (OR = 4.36, $p < 0.05$, 95 % CI = [1.226 – 15.564]), inter-digital / digital ulcer (OR = 0.073, $p < 0.05$, 95 % CI = [0.006 – 0.869]), elevated HbA1c (OR = 6.020, $p < 0.05$, 95 % CI = [1.240 – 29.226]), and higher Grade of ulcer (OR = 4.10, $p <0.1$, 95 % CI = [0.863 – 19.549]) significantly delayed wound healing.

Conclusion :

The prevalence of MDRO is alarmingly high in infected diabetic foot ulcers. Recurrent ulcers and higher grade of ulcers are more prone to acquire MDROs. MDROs in diabetic foot ulcers are associated with longer duration of hospital stay and higher rates of amputations. MDROs have no significant impact on wound healing. Presence peripheral arterial disease, osteomyelitis, nephropathy, inter-digital / digital ulcers, higher grade of ulcer and poor glycaemic control delays the healing of foot ulcer.

REVIEW OF LITERATURE

Diabetes – as old as history

Diabetes is indeed one of the oldest maladies in the history of mankind. Symptoms and suggested treatment have been mentioned in the Ebers Papyrus of 1500 B.C. Even during biblical times, gangrene of the foot has been mentioned. In Chronicles II, possibly the first case of gangrene of the foot, and in all likelihood due to diabetes, was described. Pryce, a British surgeon, more than a century ago had described the relationship between diabetic neuropathy, the insensitive foot, and foot ulceration[1].

Global burden of diabetes mellitus :

Diabetes, as per the current statistics, is known to affect in excess of 190 million people worldwide. This is likely to reach more than a quarter of a billion by 2025. Most of these could be in the developing countries. India has been considered by many as the "Diabetic capital of the world". In India alone there are over 35 million people suffering from daibetes[2]. This would more than double and be nearly 75 million by 2025, possibly as a consequence of increased life expectancy, lifestyle with lack of exercise and changing dietary patterns[3]. Insulin now being available easily, and also with therapy of diabetes being more sophisticated, patients live longer to develop the late microvascular complication of diabetes like retinopathy, nephropathy, neuropathy and peripheral vascular diseases[4] . Thus the treatment of the morbidity of diabetes poses a stiff challenge to the clinicians.

Chronic leg ulcers :

Chronic leg and foot ulcers resulting in non-healing wounds, occur because there is a disruption in the underlying physiology of the leg. This disruption has been frequently associated with venous, arterial or metabolic factors[5]. Undoubtedly these lesions lead to significant morbidity. Studies conducted in the UK have shown that, foot ulcers are approximately 1.48/1000 population [6]. There is also overwhelming evidence that this prevalence increases as the age advances [6 – 8]. In those patients over 65 years, this has been as high as 36/1000 population [9].

Diabetic foot syndrome

Diabetic foot syndrome is trinity of ulcer, infection and destruction of deep tissues of foot. Diabetic foot ulcer is one of the most common complications of diabetes, yet it is often ignored by the patients**.** Complications of diabetic foot such as ulceration and infections, apart from causing high morbidity and mortality, also have social, and economic ramifications[10-12]. 15% of all patients with diabetes have a probability of developing a foot ulcer during some stage in their lives. These ulcers are highly prone to develop infections and rapidly spread, causing significant tissue destruction leading on to some form of amputation [4,13].

Diabetic foot ulcers and amputations

There are in excess of one million amputations being done annually worldwide, with as many as 70% of them being a direct consequence of diabetes. Apart from the devastating effect of amputation on people's lives, there is also the financial burden, as foot problems being one of the commonest causes for hospitalization in people afflicted with diabtes[66]. In developing countries such as India, already with stretched health care infrastructure and resources, it has been found that this problem of diabetic foot consumes as much as 40 % of it. Patients with diabetes have a 17 times more chance of developing a gangrene of the foot, and gangrene of the lower limbs occurs in about 30% of patients with type II diabetes [14]. There is a 6.5% chance of a major amputation in patients with diabetes, which is 5 to 6 times that of a non diabetic patient. It has been found that teen ager diagnosed to have diabetes, has a very high probability of needing a major amputation by the time he reaches the sixth decade. It has also been seen that 30% to 40% of the patients with diabetes, who have had an amputation will need another amputation in the opposite limb within 3 years[15].

The mortality after one year following lower limb amputation is in the range of 11%-41%. This increases to 20%- 50% at the end of 3 years and 39%-68% at the end of 5 years[16]. St Vincent Declaration, which emerged at a meeting held under the aegis of WHO, in 1989, set a target of 50% reduction of lower limb amputations in 5 years, as a prime target in diabetes affected patients. More than 2 decades later, the target is still to be met[17], as evidenced by the fact that a lower limb is lost consequent to diabetes every half a minute[18].

Pathology of diabetic foot ulcers

A combination of neuropathy, ischemia and infection occurs, leading to an unenviable situation that poses a challenge to the health system. It can be said, treatment of diabetic foot ulcer has been improved considerably. However 1/3 to ½ of these patients may not respond to therapy[19]. There has also been significant progress in the form of re-vascularization procedures[20]. But these procedures are very skill intensive and are not accessible everywhere[18]. Newer imaging techniques like MRI, MRA [21], and introduction of new higher antibiotics, are now providing some hope[13]. However, there is the threat of infections with MRSA (methicillin-resistant staphylococcus aureus) and ESBL (extended spectrum beta lactamase) producing organisms.[22].

Diabetic foot infections : Basics

In the United States, about a quarter of all patients with diabetes are likely to develop foot ulcerations at some point, and a majority of these run the risk of becoming infected[33]. The association of bacteria with ulcer can be classified into four types : contamination, colonization, critical colonization and infection. Contamination and colonization are milder forms of microbial invasion and do not cause a detrimental effect in the process of healing. When this begins to adversely affect the process of wound healing, the term 'critical colonization' is used [23]. The Consensus Development Conference on Diabetic Foot Wound Care [24] agreed that an ulcer should be deemed infected when there are purulent secretions or the presence of two or more signs of inflammation (erythema, warmth, tenderness, heat, induration). All chronic wounds, however by their very nature of chronicity, may not always show these above mentioned classic features of infection. It has been therefore suggested that the list should be expanded and should include signs specific to secondary wounds (serous

exudate associated with concurrent inflammation, delayed healing, discoloration of granulation tissue, friable granulation tissue, foul odour and wound breakdown)[25].

Microbiologically, the indicators of infection proposed are a critical bacterial load, an interplay between multiple bacterial species infecting simultaneously, and the presence of specific pathogens. It can be said that that the mere presence of bacteria does not indicate wound infection. It is now known that there is a direct effect of critical microbial load on the healing outcome of both acute and chronic wounds[26]. There is definite evidence that wounds do not heal when there is a bacterial load in excess of 10^5 bacteria per gram of tissue[27].

Microorganisms have been identified in the deeper layers of all chronic wounds. However, their role and the effect of specific species of bacteria on wound healing are yet to be elucidated. All chronic wounds are colonized. Microbial study can be useful only when considered in conjunction with clinical features, to identify the bacteriae causing infection and their antibiotic sensitivities [28,29]. This should lead to an improved antibiotic regimen[28].

Diabetic foot infections – Treatment challenges :

Highlighting the difficulties for the clinician, the International Working Group on the Diabetic Foot recommended a complex antibiotic strategy which involves intravenous and/or possibly oral use of empirical broad-spectrum antibiotics in the presence of deep foot infections[30]. The recommendations include ampicillin/sulbactam, ticarcillin/clavulanate, co-amoxiclav, clindamycin and a quinolone, second or third generation cephalosporin and a quinolone, and metronidazole with a quinolone [30]. It has been recommended that only ulcers with extensive cellulitis and/or osteomyelitis should be treated with intensive, systemic antibiotics[31]. When wounds are infected with more than one bacteria, it would be necessary to

use a broad spectrum antibiotic, but there is as yet no final word on which antibiotic to use as there is inadequate evidence to show that one is better than the other[31]. Proper management of these infections requires appropriate antibiotic selection based on culture and antibiotic susceptibility results [32].

Bacteriology of diabetic foot infections :

Wounds are treated initially with an empirical antibiotic. Treatment with a specific antibiotic based on antibiotic sensitivity test, should be instituted to improve the healing. Many studies have reported varied and contradictory results. Literature review has shown that Staphylococcus aureus is the main etiological pathogen [22,34,35]. Two recent studies reported gram-negative aerobes being the predominant pathogens [11,12]. Etiological pathogens have varied over time and geographical location [11, 12, 36]. It is interesting to note, when specimens are collected properly, transported promptly and validated culture techniques are used, polymicrobial isolates are usually obtained from diabetic foot infections[5, 37, 38, 39, 40, 41, 42]. Furthermore, some studies have shown that when the wounds have polymicrobial infections there is a synergism of these organisms, as a result of which, virulence factors, such as hemolysins, proteases, and collagenases are produced. These are detrimental to wound healing and result in infections becoming chronic [43, 44, 45, 46]. There is also a formation of a biofilm, which thwarts the entry of antibiotics into the infected site [47]. It can therefore be said that polymicrobial infections can have challenging clinical ramifications [38,43].

Recent studies using molecular techniques have emphasized the complex ecology of these wounds [48,49]. The average number of bacterial species per ulcer has been found to be in the range of 1.6 up to 4.4 [50 – 53]. Another interesting point to note that even when ulcers do not show any clinical sign of infection, more than one bacterial species has been isolated [54].

In a Malaysian study, 287 bacteriae were isolated from 194 patients. This showed an average of 1.47 isolates per patient. Gram negative bacteria (52 %) were most frequently isolated. Among these gram negative bacteria, proteus spp. (28%), pseudomonas aeruginosa (25%), klebsiellapneumoniae (15%) and Escherichia coli (9%) were isolated commonly. Among the Gram-positive bacteria most common organism isolated was Staphylococcus aureus (44 %),followed by Group B streptococci (25%) and Enterococcus spp (9%). The antibiogram of these isolates showed that the gram negative bacteria were sensitive to imipenem and amikacin and the gram positive bacteria were sensitive to vancomycin.[64].

A Chennai study showed aerobic pathogens were isolated in 66.8% patients and anaerobic pathogens were isolated in 33.2%. There was a greater isolation of anaerobic pathogens with higher Wagner's grade ulcers. These ulcers which were infected with anaerobic pathogens, took longer to heal. Neuropathy was common in patients infected with both aerobic and anaerobic pathogens. The two groups showed no significant difference in associated peripheral vascular disease. Among the aerobic pathogens isolated, enterobacteriaceae (48%) was the commonest. Staphylococcus spp (18.2%), streptococcus spp (16.8%) and pseudomonas spp (17%) were the other aerobic isolates seen frequently. Anaerobes isolated were peptostreptococcus spp and clostridium spp (69.4%). Further, gram-negative anaerobes like bacteroides spp and fusobacterium spp were present in 30.6%. Strict aerobic pathogen and strict anaerobic pathogen infected ulcers had a longer healing time[65].

Multi drug resistant organisms(MDRO) and diabetic foot ulcers :

Many different definitions for multidrug-resistant (MDR) bacteria have emerged in the literature to outline the different patterns of resistance seen. European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC), created standardized international criteria, using which multi-drug resistance profiles could be identified in Staphylococcus aureus, E*nterococcus* spp, *Enterobacteriaceae*(other than *Salmonella* and *Shigella*),*Pseudomonas aeruginosa*, and *Acinetobacter* spp. All these bacteria have often let to multidrug resistance [67].

Clinicians are often challenged by the lethal combination of increasing numbers of patients with chronic wounds and with the rising problem of multi antibiotic resistance. The polymicrobial infection of chronic wounds provides an ideal ambience for exchange of genetic material between bacteria.

In the United States, the first two cases of vancomycin resistant Staphylococcus aureus were both isolated from patients with chronic wounds [55,56]. A study found more than 50 % of Staphylococcus aureus isolates from patients admitted to dermatology wards with leg ulcers to be Methicillin Resistant Staphylococcus Aureus (MRSA). Further more than one-third of Pseudomonas aeruginosa isolates were found to be resistant to ciprofloxacin[57]. Another study found 40% of Staphylococcus aureus isolated from non-limb-threatening infected foot ulcers to be MRSA; giving MRSA a prevalence of 15% in all diabetic patients with infected ulcers[50].

There were significantly increased MRSA isolates from patients who had received previous antibiotic therapy. A follow-up study, identified a similar proportion of methicillin resistance in the Staphylococcus aureus isolates, but showed that it had almost doubled to 30 % over a 3 year period [22].

Microbial isolates from infected diabetic foot ulcers, who had received no prior antibiotics during the previous two weeks, found 12% of Staphylococcus aureus, 46% of Staphylococcus epidermidis and 45% of Staphylococcus haemolyticus to be methicillin resistant[58]. High resistance was found to erythromycin in most species of gram-positive organisms. An audit of chronic wounds found 12.5% of Staphylococcus aureus isolates and 21.7% of Pseudomonas species isolates to be resistant to a clinically relevant antibiotic[59].

Literature has found MRSA in as many as 15–30% of diabetic wounds [4,11,32,50]. Suggested risk factors for MRSA include cross-contamination of wounds from the patients themselves, fomites or health care professionals, prolonged use of antibiotics, previous hospitalization and illness severity[61,63]. Infection with multidrug-resistant organisms (MDROs) may increase the morbidity and mortality, the duration of hospital stay and the cost of treatment[60]. High prevalence of antibiotic resistance, like MRSA, suggests that empirical antibiotics may not cover these resistant organisms [62].

Ulcers infected with MRSA take twice as much time to heal [50]. There is as yet no consensus on the relevance of MRSA colonization in clinically non-infected ulcers, though it has been seen it may take upto six months to disappear [22].

A study from New Delhi had found that on an average 2.3 species were isolated from each ulcer. The majority (65.0%) were infected with aerobes only. Staphylococcus aureus was the most frequent pathogen, found in nearly 14% of infections. Staphylococcus aureus showed a high frequency (56.0%) of resistance to the antibiotics tested. ESBL production was seen in

44.7% of gram-negative bacilli, Proteus species showing the highest production followed by Escherichi coli. MDRO were isolated from more than two-thirds of the ulcer. Patients with non MDROs had a higher frequency of hypertension, and this was the only factor significantly associated with it. Both MDROs and Non MDROs had a similar duration of hospital stay, and showed no significant differences in the demographic pattern. An ulcer of size of >4 cm^2 was more likely to be infected with MDROs. Patients with MDRO ulcers had neuropathy and osteomyelitis more frequently. MDROs had a higher association with peripheral vascular disease, association however, had only a borderline significance. Significantly, surgical treatment was required more in patients with MDRO infections. Multiple logistic regressions showed a high degree of association between presence of neuropathy and ulcer size > 4 cm^2 [12].

In a study done at Aligarh, India, gram negative aerobes were most frequently isolated (63.8%), followed by gram positive aerobes (36.1%). Anaerobes were isolated in 31.4%. 45% of patients showed MDROs. ESBL production and methicillin resistance were noted in 68.5% and 43.2% of bacterial isolates respectively. MDRO positive status was associated with the presence of neuropathy, osteomyelitis, and ulcer size >4 cm^2, but not with patients characteristics like age, sex, ulcer type and type of diabetes, or duration of hospital stay [64].

In a study done at France by Hartemann-haurier et al[60], 18% of admission specimens were positive for MDRO. There was no association of MDRO-positive status with the patient profile (age, sex, type of diabetes, complications of diabetes), duration of wound, or type of wound (neuropathic or ischaemic). Multivariate analysis showed that, the only two factors associated significantly with positive MDRO status were, a history of prior hospitalization for the same ulcer and the presence of osteomyelitis. MDRO-positive status either on admission or during follow-up had no association with time to healing.

The study from UK, has found that Staphylococcus aureus being the commonest isolate. 30.2% of patients with foot ulcers harboured MRSA. They also found that there was no increase in hospitalisation as a consequence of MRSA and it is not related to previous antibiotic usage.[22]

The increasing antimicrobial resistance is a conundrum to clinicians and microbiologists alike. In India however there is a lack of literature on the frequency of MDRO infections and the consequences of such infections in patients with diabetic foot ulcers.

METHODOLOGY

This study is a prospective observational study conducted to find the prevalence, risk factors and the impact of multidrug resistant organisms in diabetic foot ulcers. It was conducted during the months January 2011 to July 2012 at PSG Institute of Medical Sciences & Research, Coimbatore.

150 diabetic patients with foot lesions were included in the study. Written informed consents were obtained from the patients. Detailed clinical history of the patient and other relevant data were collected using structured case report forms.

Mode of presentation of foot ulcers were classified as grade I – V as per Meggit Wagner Classification System (Wagner,1981). Ulcers were categorised into necrotic / non necrotic ulcers based on signs of infection (swelling, exudates, surrounding cellulitis, odour, tissue necrosis and crepitation). Size was determined by multiplying the longest and widest diameters expressed in centimeters squared (cm2), and the diagnosis of extension to the bone was made by plain radiographs.

Presence of neuropathy was detected by assessing vibration sensation using a 128 HTZ tuning fork and a 10g Semmes - Weinstein monofilament. Peripheral diabetic neuropathy was defined as an abnormal monofilament test, as described by the international consensus on the diabetic foot[102]. Presence of nephropathy was detected by screening the patient's urine for micro / macro-albuminuria after ruling out urinary tract infection.

The fundus was examined by the ophthalmologist for evidence of retinopathy. Absence of both dorsalis-pedis pulsations and / or an Ankle Brachial Index (ABI) less than 0.9 was termed as peripheral vascular disease[101].

Wound swabs were obtained from the floor of the ulcer, before starting on empirical antibiotic therapy. Direct microscopic examination and aerobic cultures were done by standard methods. The bacteriological spectrum and the sensitive antibiotics were noted for each patient.

All patients were started on empirical antibiotics depending on the status of the wound. In mild infection amoxyclav (amoxicillin/clavulanic acid) was given by oral route. But in patients with necrotic wounds, an additional antibiotic, clindamycin or metronidazole, was added for gram negative coverage and the intravenous route was preferred.

In the presence of an unhealthy ulcer, surgical debridement / amputation was done immediately after admission. Later wounds were managed with regular dressings and antibiotics modified according to the culture report. All patients were re-inspected or enquired over phone after a period of 10 weeks to assess the status of wound.

For each patient the following details were entered: age, sex, duration of ulcer, duration of diabetes, glycaemic control, presence of retinopathy, presence of micro/macro-albuminuria, hypertension, history of smoking, history of previous amputation, duration of hospital stay, interventions (medical and surgical), organisms cultured from ulcer, antibiotic profile and status of ulcer after 10 weeks.

Previous hospitalization was defined as any hospital stay, which was not necessarily for the management of ulcer, during the year preceding the current hospitalization. Previous

antibiotic usage was defined in our study, as those who had received antibiotics in six months preceding current hospitalization.

The data was collected and entered in the SPSS data sheet.The data was analyzed using SPSS 20 for descriptive statistics. To assess the risk factors for acquiring MDRO, the patients were grouped into MDRO and non-MDRO groups. All patients who had at least one multidrug resistant organism were grouped under MDRO group.

The test variables were compared using Chi-square test for qualitative variables and Student's test for quantitative variables. The variables for which the association was statistically significant ($p< 0.1$) were introduced in a logistic model to explain the presence of MDRO. The impact of multi-drug resistant organisms was assessed by analyzing the mean duration of hospital stay and its association with amputations, using the above said statistical tools.

For analyzing the factors influencing the wound healing, the patients were grouped into two groups: healed and non-healed group. At 10 weeks time, the completely healed ulcers or those which had reduced in size were deemed to have healed. The rest, including those with ulcers, whose size remained the same were grouped as non-healed group. Influence of various factors were analyzed using same statistical tools.

Methodology	
Aim	• To study the prevalence of multi-drug resistant organism infection in diabetic foot ulcers. • To analyze the risk-factors contributing to infection with multidrug resistant organisms. • To assess the impact of MDRO infection on ulcer healing. • To analyze other factors influencing wound healing
Study design:	A Prospective Hospital based Observational study
Study Population:	All diabetic patients (both IP & OP) with foot lesions over a period (Jan 2011 – July 2012) were included in the study.
Sample Size:	150
Inclusion Criteria	All diabetic patients with foot lesions

Methodology	
Exclusion Criteria:	➢ Diabetic patients with pure venous ulcers ➢ Those patients with neurological disorders and other known causes of neuropathy, other than diabetes related neurological dysfunction will be excluded from the study ➢ Those who do not consent
Duration of the study	18 months
Study Period	January 2011 - July 2012

CLINICAL PROFORMA

Name : Age : Sex :

IP No : OP No :

DOA : DOD : Duration of Stay : days

Occupation : Per-Capita Income :

Mobile Number :

Diabetic Status :

Type of diabetes : Type I [ ]
Type II [ ]

Duration - yrs, Newly Detected [ ]

Latest HbA1C : %

Smoking History : Yes [ ]
No [ ]

Alcoholism : Yes [ ]
No [ ]

Nature of work : Manual [ ]
Sedentary [ ]

Other concomitant Illness : HT [ ]
Nephropathy [ ]
Retinopathy [ ]

Past history of amputations for foot problems : Yes [ ]
No [ ]

Previous hospitalization for the same complain : Yes [ ]
No [ ]

How many years back ----
Reason for hospitalization ----

Previous antiobiotic usage : Yes [ ]

No [ ]

Recurrent ulcer : Yes [ ]

No [ ]

Local examination of the foot lesion:

Ulcer :

Size –
Depth –

Duration of ulcer :

Osteomyelitis : present / Absent

Nature : Necrotic / Non-necrotic

Site :

Wagner's Grade :

Evidence of peripheral vascular disease :

Dorsalispedis Artery Palpable : Yes [ ] No [ ] Impaired [ ]

Posterior tibial Artery palpable : Yes [ ] No [ ] Impaired [ ]

Ankle brachial index _____

Assessment of sensorimotor Neuropathy : Monofilament test : present [ ]

Absent [ ]

Culture : Monomicrobial [ ]

Polymicrobial [ ]

Organisms :

MDRO : Present [ ]

Absent [ ]

Antibiotics used :

Treatment during the hospital stay :

Duration of hospital stay :

Follow up :

At ten weeks :

RESULTS

150 diabetic in-patients with foot ulcers were included in the study, after obtaining their consent. 78% of the patients were 51 years or older, with the average age being 58.21. 74.6% of the patients were males, showing a distinct male preponderance. Most of the patients (44%) belonged to class II socio-economic status followed by class III (26 %), as per Modified Prasad's Classification[103]. No patients were in class V socio-economic status. (Table 1)

Table 1: Demographic details

Variable	Number	Percentage
AGE DISTRIBUTION		
< 40	5	3.3 %
41 – 50	16	10.7 %
51 – 60	55	36.7 %
61 – 70	62	41.3 %
71 – 80	10	6.7 %
81 – 90	2	1.3 %
SEX DISTRIBUTION		
MALE	112	74.6 %
FEMALE	38	25.33 %
SOCIO-ECONOMIC STATUS		
Class I	39	26 %
Class II	66	44 %
Class III	39	26 %
Class IV	6	4 %
Class V	0	0 %

Almost all the patients had Type II diabetes, with only 4% of them having Type I. Only 19.33% of patients had a good glycemic control, with HbA1c 6 – 7 %. 40 % of patients with ulcer had diabetes for less than 5 yrs. (Table 2)

Table 2: Diabetes profile

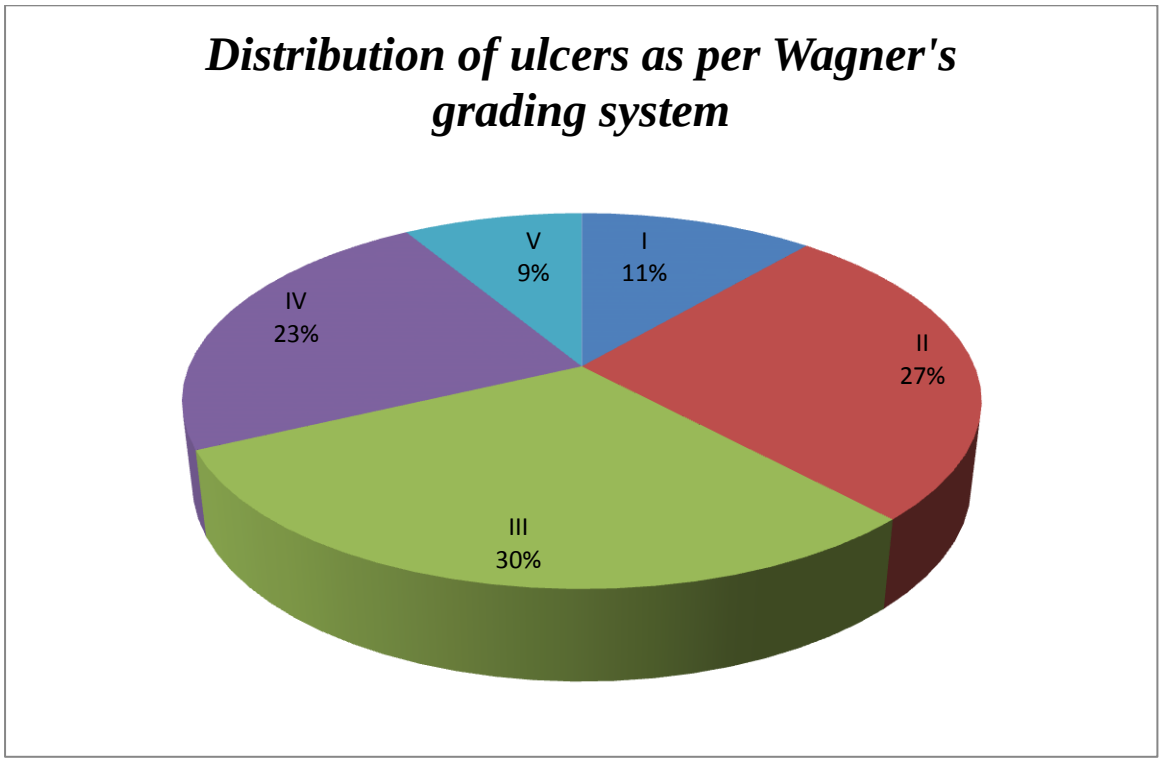
Variable	Number	Percentage
DURATION OF DIABETES		
< 5 YRS	60	40 %
5-10 YRS	51	34 %
10-15 YRS	26	17 %
15 – 20 YRS	11	7.3 %
>20 YRS	2	1.3 %
GLYCEMIC CONTROL		
6-7 % (Good)	29	19.33 %
7-8 % (Fair)	54	36 %
>8 % (Poor)	67	44.66 %

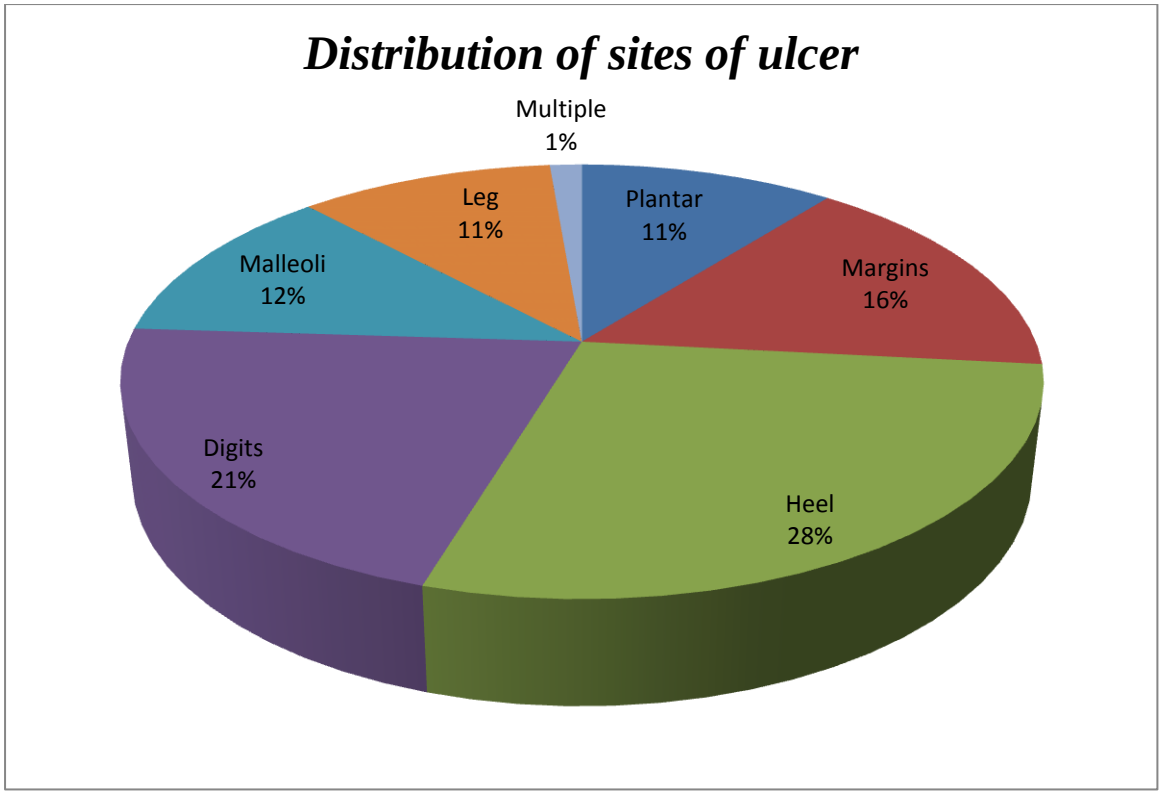
68 % of patients had ulcers of less than one month duration. Less than 10% of the ulcers studied had a duration of 2 months or greater. With respect to the size of the ulcer, most were between 4 to 8 cm^2 and 8 to 16 cm^2. A majority had superficial ulcers. Most of the patients had Wagner's grade II, III, or IV ulcers. It was interesting to note that there were very few ulcers with Wagner's grade V. There was almost an equal distribution of necrotic and non-necrotic ulcers. Similarly recurrent and non-recurrent ulcers also had an almost equal distribution. 34% of ulcers had associated osteomyletis. As far as the site of the ulcer was concerned, 28% were seen in the heel, followed by digits / inter digital areas (21.33 %). (Table 3)

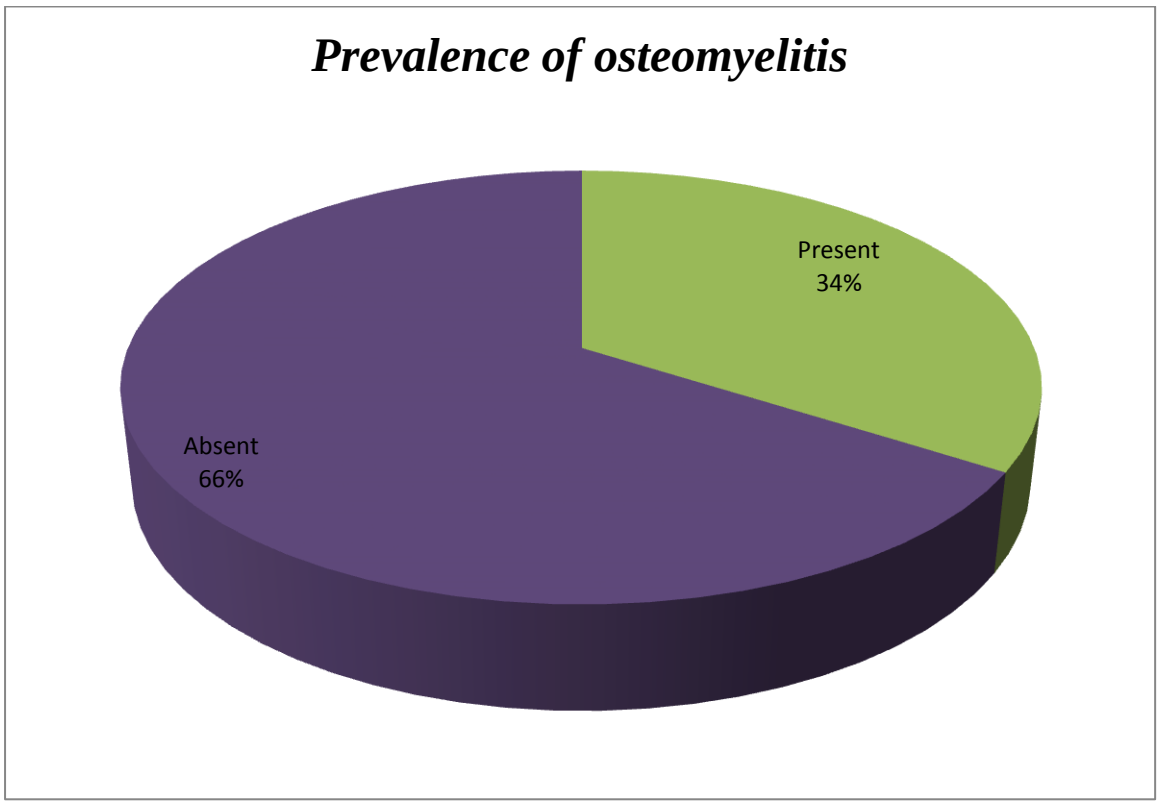
Table 3: Foot ulcer profile

Variable	Number	Percentage
DURATION OF ULCER		
<1 Month	102	68 %
1-2 Months	34	22.7 %
2-3 Months	9	6 %
>3 Months	5	3.3 %
SIZE OF THE ULCER		
<4 cm^2	11	7.3 %
4-8 cm^2	49	32.7 %
8-16 cm^2	61	40.7 %
16-24 cm^2	23	15.3 %
>24 cm^2	6	4 %
DEPTH OF ULCER		
Superficial	92	61.33 %
Deep	58	38.66 %
GRADE OF ULCER		
Grade I	17	11.33 %
Grade II	40	26.66 %
Grade III	45	30 %
Grade IV	35	23.33 %
Grade V	13	8.66 %
NATURE OF ULCER		
Non-necrotic	78	52 %
Necrotic	72	48 %
RECURRENCE		
Non-recurrent	79	52.66 %
Recurrent	71	47.33 %
OSTEOMYELITIS		
Absent	99	66 %
Present	51	34 %

Variable	Number	Percentage
SITE OF ULCER		
Plantar	16	10.66 %
Margins	24	16 %
Heel	42	28 %
Digits	32	21.33 %
Malleoli	18	12 %
Leg	16	10.66 %
Multiple areas	2	1.33 %




Distribution of sites of ulcer
Multiple
1%
Plantar
11%
Margins
16%
Heel
28%
Digits
21%
Malleoli
12%
Leg
11%


Prevalence of osteomyelitis
Present
34%
Absent
66%

Wagner's Grade 1 Ulcer

Superficial Diabetic ulcer

Wagner's Grade 2 Ulcer

Ulcer involving Ligament, Tendon or Fascia without abscess/osteomyelitis

Wagner's Grade 3 Ulcer



Deep ulcer with abscess/osteomyelitis

Wagner's Grade 4 Ulcer

Gangrene of a part of Foot

Wagner's Grade 5 Ulcer

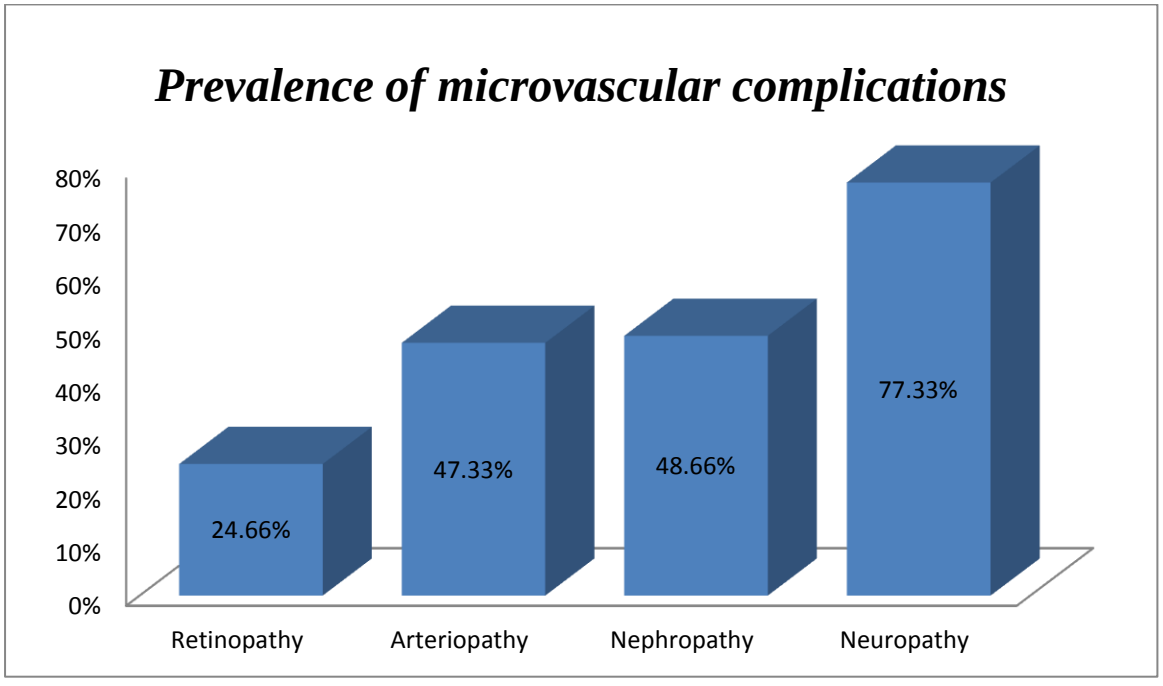
Extensive Gangrene of the Foot

Peripheral arterial disease was seen in 52.66 %, retinopathy detected in 24.66 % and albuminuria suggesting nephropathy was found in 48.66 %. Majority of the patients had neuropathy. 61.33 % were hypertensive. 50% of the patients were smokers and 41.33 % alcoholics. History of previous hospital admission in the last one year was seen in 53.33 %. 21.33 % of patients had history of some form of amputation. 42.66 % of the patients had a history of antibiotic use in the preceding 6 months before admission. (Table 4).

Table 4: Other associated history

Variable	Number	Percentage
ARTERIOPATHY		
Absent	79	52.66 %
Present	71	47.33 %
RETINOPATHY		
Absent	113	75.33 %
Present	37	24.66 %
NEPHROPATHY		
Absent	77	51.33 %
Present	73	48.66 %
NEUROPATHY		
Absent	34	22.66 %
Present	116	77.33 %
HYPERTENSION		
Absent	58	38.66 %
Present	92	61.33 %
SMOKING		
Non smoker	75	50 %
Smoker	75	50 %

Variable	Number	Percentage
ALCOHOL Non alcoholic Alcoholic	 88 62	 58.66 % 41.33 %
PREVIOUS HOSPITALIZATION Not hospitalized Hospitalized	 70 80	 46.66 % 53.33 %
H/O AMPUTATION Absent Present	 118 32	 78.6 % 21.33 %
PREVIOUS ANTIBIOTIC USE Absent Present	 86 64	 57.33 % 42.66 %

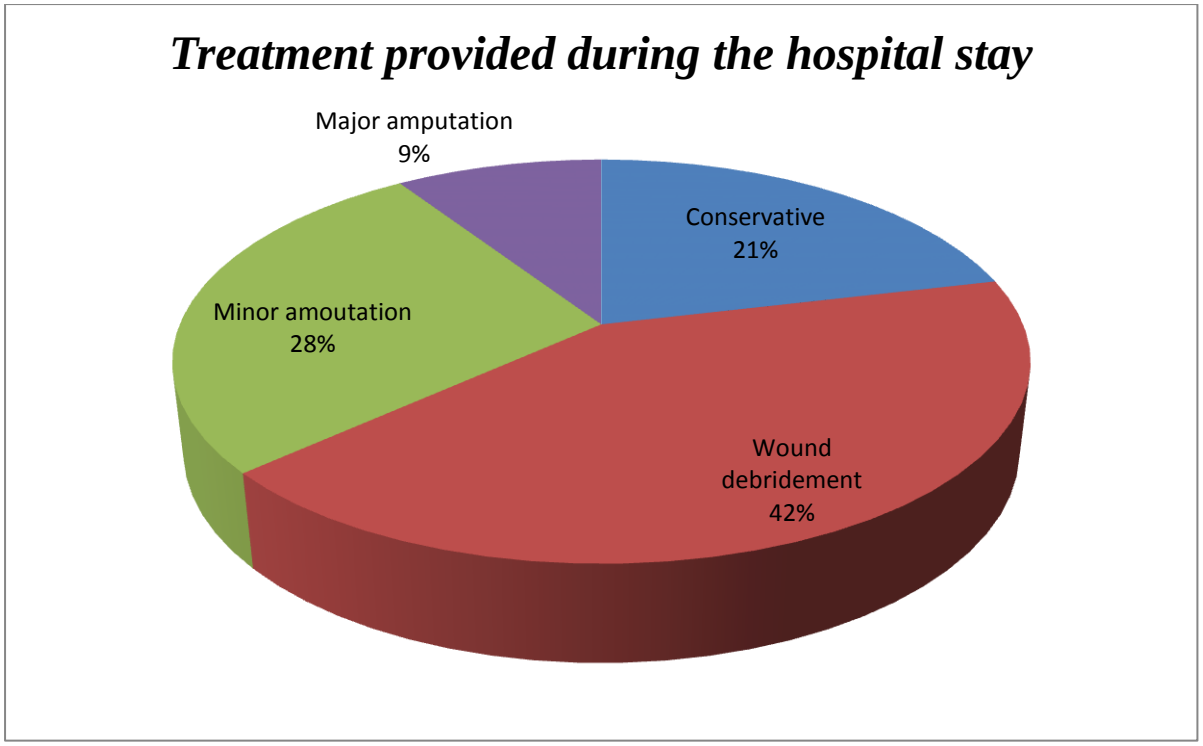


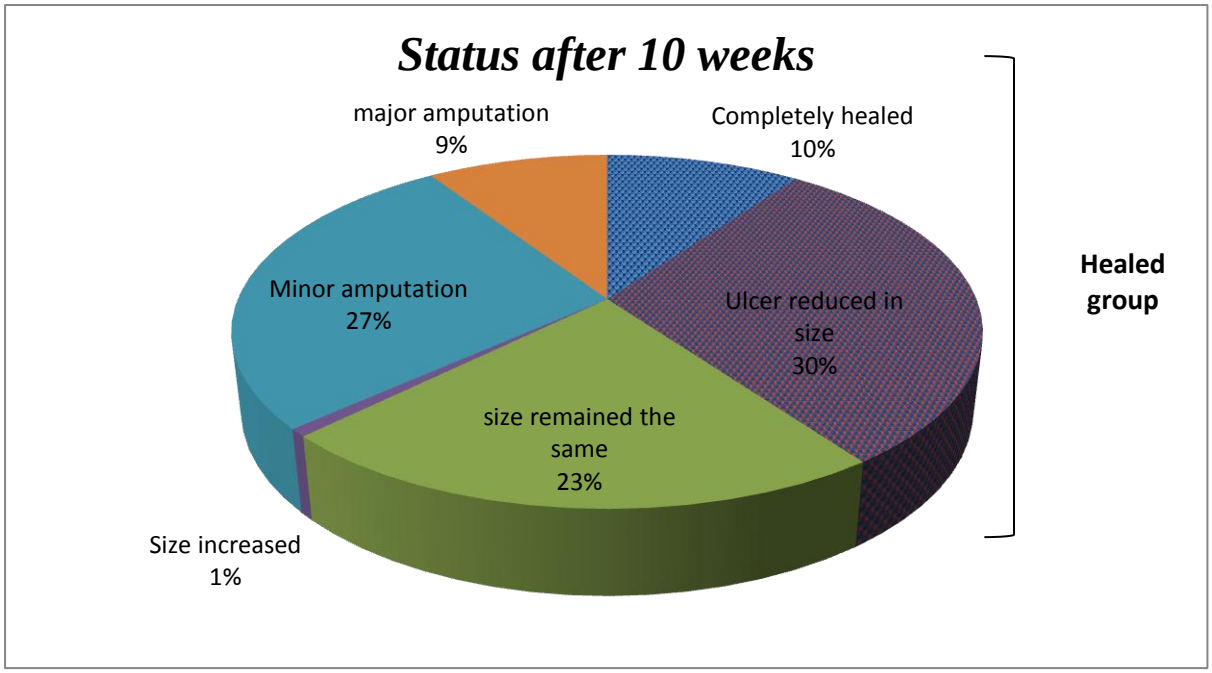
42 % of patients required wound debridement and more than a third of the patients underwent some form of amputation. 32 of the 150 patients (21,3%) had only conservative treatment.

All patients were followed up at 10 weeks, 40 % of the patients had ulcers either healed or reduced in size. The rest had either an increase in size of the ulcers or had some form of amputation. (Table 5)

Table 5: Management

Variable	Number	Percentage
MANAGEMENT OF ULCER		
Conservative	32	21.3 %
Wound debridement	63	42 %
Minor amputation	41	27.3 %
Major amputation	14	9.3 %
10 WEEKS FOLLOW UP		
Completely healed	15	10 %
Ulcer reduced in size	45	30 %
Size remained the same	34	22.7 %
Ulcer size increased	1	0.7 %
Minor amputation	41	27.3 %
Major amputation	14	9.3 %


Treatment provided during the hospital stay
Major amputation
9%
Conservative
21%
Minor amoutation
28%
Wound
debridement
42%


Status after 10 weeks
major amputation
9%
Completely healed
10%
Minor amputation
27%
Ulcer reduced in
size
30%
size remained the
same
23%
Size increased
1%
Healed
group

MICROBIOLOGICAL OBSERVATIONS :

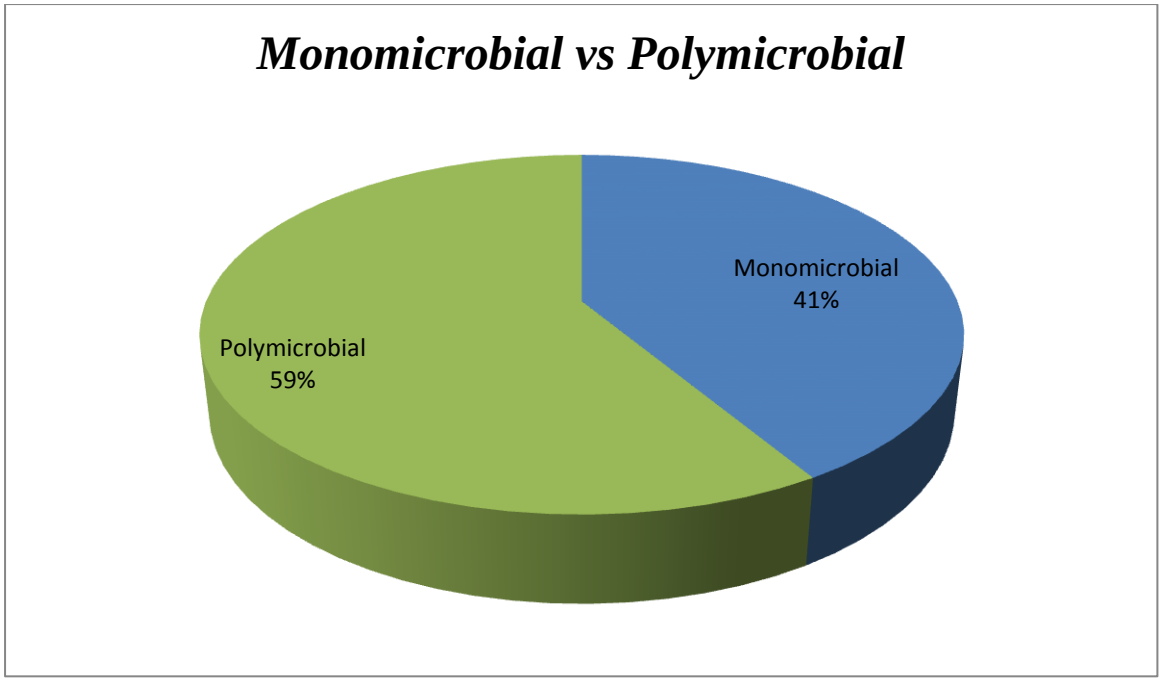
A total of 279 organisms were isolated from 150 patients. On an average 1.86 species were isolated from each patient. 58.66 % of patients (88 of the 150 patients) had polymicrobial culture. Among the isolates, most were gram negative rods (69.89 %) and almost all the rest were gram positive cocci. There was a solitary gram negative coccus. Gram positive to gram negative ratio, among the isolates, was 1: 2.3.

Among the isolates, Escherichia coli was the most common one constituting 17.9%, followed by Staphylococcus aureus 17.6 %, followed by Pseudomonas aureginosa (16,5%).

Multidrug resistance in the organisms, was defined as per the criteria laid down by European centre for Disease Prevention and Control[67]. Multidrug resistance organisms were seen in 99 of the 150 patients. (Tables 6 & 7)

Table 6: Bacteriology overview

	Number of patients	**Percentage**
CULTURE		
Mono-microbial	62	41.33 %
Poly-microbial	88	58.66 %
DRUG RESISTANCE		
MDRO	99	66 %
NON- MDRO	51	34 %


Monomicrobial vs Polymicrobial
Monomicrobial
41%
Polymicrobial
59%

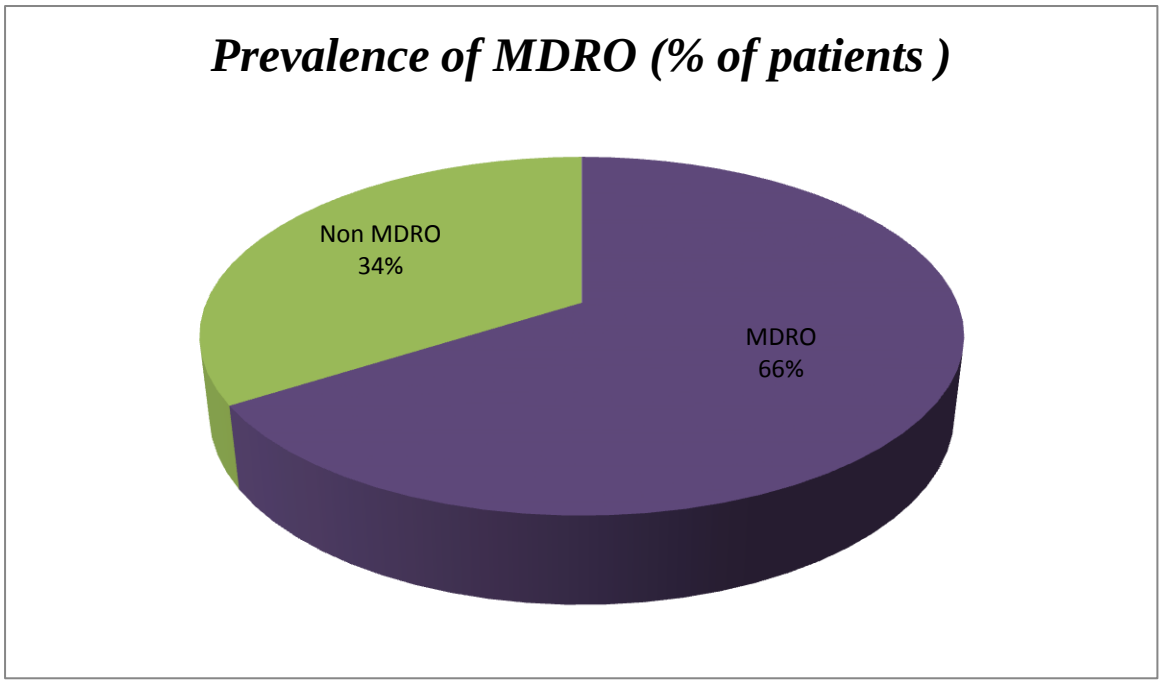
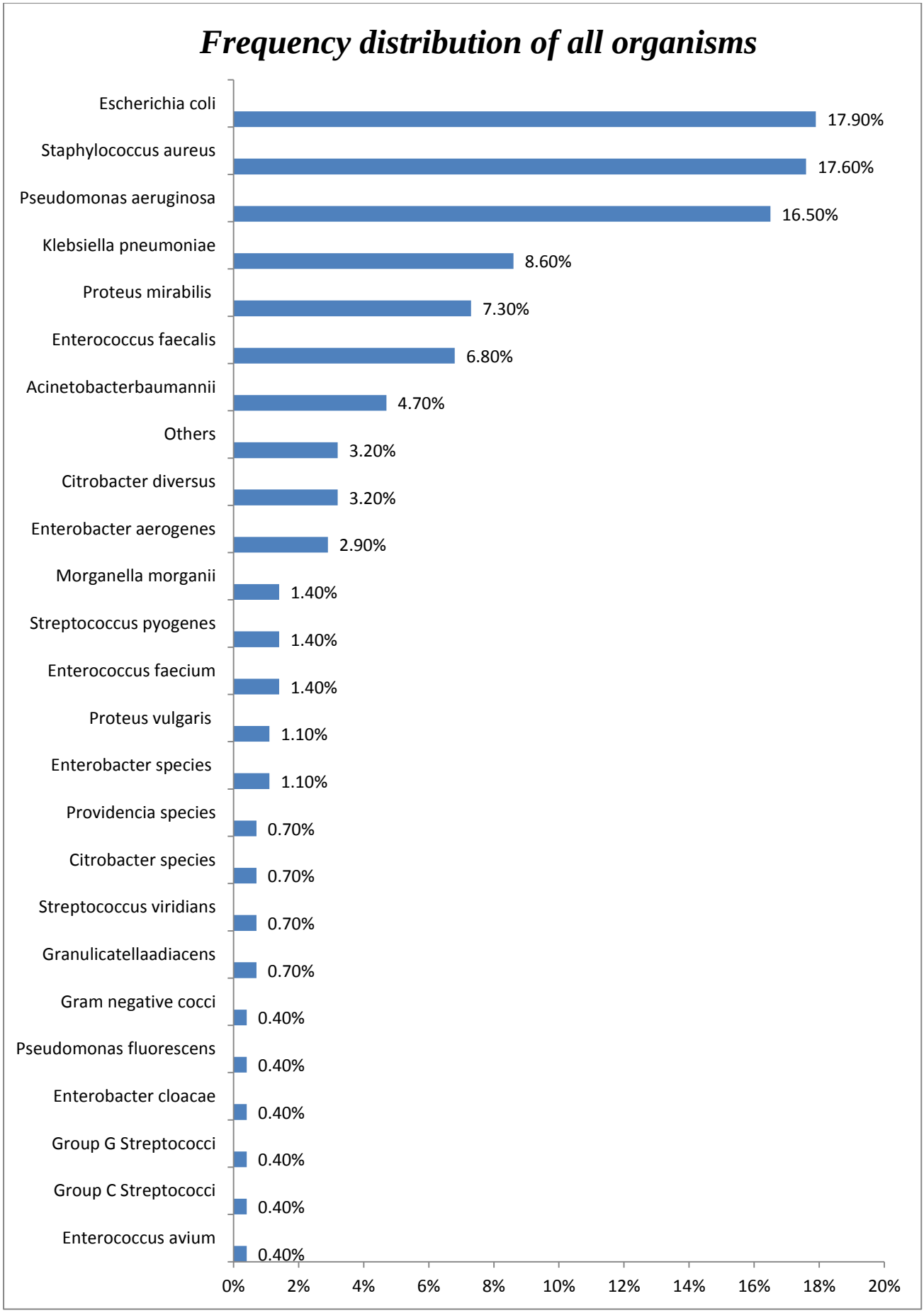

Prevalence of MDRO (% of patients)
Non MDRO
34%
MDRO
66%

Table 7: List of isolated organisms

ORGANISMS	N	PERCENT OF ISOLATES	PERCENT OF CASES
GRAM- POSITIVE COCCI			
Enterococcus avium	1	0.4 %	0.7 %
Enterococcus faecalis	19	6.8 %	1 2.7 %
Enterococcus faecium	4	1.4 %	2.7 %
Granulicatellaadiacens	2	0.7 %	1.3 %
Staphylococcus aureus	49	17.6 %	32.7 %
Group C Streptococci	1	0.4 %	0.7 %
Group G Streptococci	1	0.4 %	0.7 %
Streptococcus pyogenes	4	1.4 %	2.7 %
Streptococcus viridians	2	0.7 %	1.3 %
Total	**83**	**29.8 %**	
GRAM-NEGATIVE RODS			
Acinetobacter baumannii	13	4.7 %	8.7 %
Citrobacter diversus	9	3.2 %	6.0 %
Citrobacter species	2	0.7 %	1.3 %
Enterobacter aerogenes	8	2.9 %	5.3 %
Enterobacter cloacae	1	0.4 %	0.7 %
Enterobacter species	3	1.1 %	2.0 %
Escherichia coli	50	17.9 %	33.3 %
Klebsiella pneumoniae	24	8.6 %	16 %
Morganella morganii	4	1.4 %	2.7 %
Proteus mirabilis	20	7.3 %	13.4 %
Proteus vulgaris	3	1.1 %	2.0 %
Pseudomonas aeruginosa	46	16.5 %	30.7 %
Pseudomonas fluorescens	1	0.4 %	0.7 %
Providencia species	2	0.7 %	1.3 %
Others	9	3.2 %	6.0 %
GRAM-NEGATIVE COCCI	1	0.4 %	0.7 %
Total	**196**	**70.5 %**	
GRAND TOTAL	**279**	**100 %**	


Frequency distribution of all organisms
Escherichia coli
17.90%
Staphylococcus aureus
17.60%
Pseudomonas aeruginosa
16.50%
Klebsiella pneumoniae
8.60%
Proteus mirabilis
7.30%
Enterococcus faecalis
6.80%
Acinetobacterbaumannii
4.70%
Others
3.20%
Citrobacter diversus
3.20%
Enterobacter aerogenes
2.90%
Morganella morganii
1.40%
Streptococcus pyogenes
1.40%
Enterococcus faecium
1.40%
Proteus vulgaris
1.10%
Enterobacter species
1.10%
Providencia species
0.70%
Citrobacter species
0.70%
Streptococcus viridians
0.70%
Granulicatellaadiacens
0.70%
Gram negative cocci
0.40%
Pseudomonas fluorescens
0.40%
Enterobacter cloacae
0.40%
Group G Streptococci
0.40%
Group C Streptococci
0.40%
Enterococcus avium
0.40%
0%
2%
4%
6%
8%
10%
12%
14%
16%
18%
20%

As stated earlier, the frequency distribution of patients with multidrug resistant organisms among the 150 patients included in the study, was 66%, being observed in 99 out of 150 patients. 54.8 % (153 out of 279) of isolated organisms were multidrug resistant organisms.

Antibiotic resistance was observed in 58.6% (115 out 196) of gram negative organisms compared to 45.78% (38 out of 83) in gram positive organisms. Among the gram positive cocci, 55 % of Staphylococcus aureus species and 47.36 % of Enterococcus faecalis species were multidrug resistant.

Among the gram negative bacilli, multidrug resistance was noted in 78% of Escherichia coli, 74% of Pseudomonas auroginosa, 70% of Proteus mirabilis and 61.53% of Acinitobacter baummanni, with lower percentages in other isolates. Listing the multidrug resistant organisms isolated, MDR Pseudomonas aeruginosa was found to be the highest (34/153), followed by ESBL Escherichia coli (33/153).

However, when the number of ESBL + Amp C Escherichia coli are considered together along with ESBL Escherichia coli, this would be the highest. (Tables 8&9)

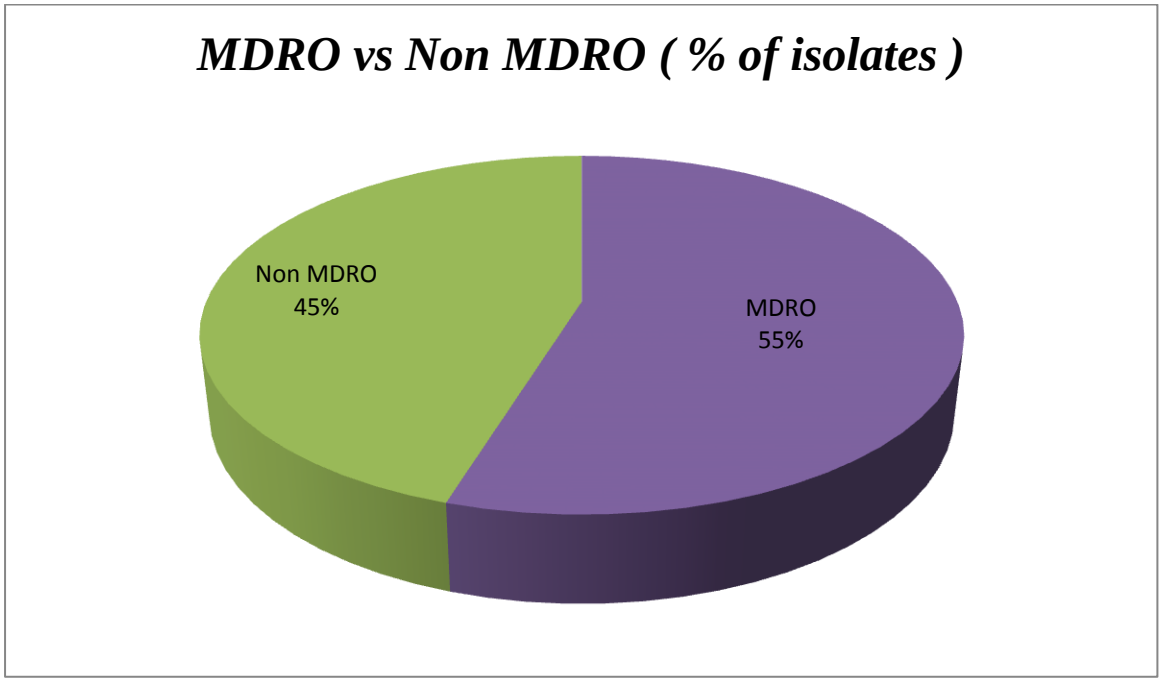


Table 8: Frequency distribution of multidrug resistant organisms

ORGANISMS	N (%)	MDRO N (%)	Ulcers with MDRO (%)
GRAM- POSITIVE COCCI			
Enterococcus avium	1 (0.4%)	1 (100%)	0.66%
Enterococcus faecalis	19 (6.8%)	9 (47.36%)	6%
Enterococcus faecium	4 (1.4%)	1 (25%)	0.66%
Granulicatella adiacens	2 (0.7%)		
Staphylococcus aureus	49 (17.6%)	27 (55%)	18%
Group C Streptococci	1 (0.4%)		
Group G Streptococci	1 (0.4%)		
Streptococcus pyogenes	4 (1.4%)		
Streptococcus viridans	2 (0.7%)		
GRAM-NEGATIVE RODS			
Acinetobacter baumannii	13 (4.7%)	8 (61.53%)	5.3%
Citrobacter diversus	9 (3.2%	3 (33.33%)	2%
Citrobacter species	2 (0.7%)		
Enterobacter aerogenes	8 (2.9%)	3 (37.5%)	2%
Enterobacter cloacae	1 (0.4%)		
Enterobacter species	3 (1.1%)		
Escherichia coli	50 (17.9%)	39 (78%)	26%
Klebsiella pneumoniae	24 (8.6%)	10 (41.66%)	6.6%
Morganella morganii	4 (1.4%)	2 (50%)	1.3%
Proteus mirabilis	20 (7.3%)	14 (70%)	9.3%
Proteus vulgaris	3 (1.1%)		
Pseudomonas aeruginosa	46 (16.5%)	34 (74%)	22.6%
Pseudomonas fluorescens	1 (0.4%)		
Providencia species	2 (0.7%)	2 (100%)	1.3%
Others	9 (3.2%)		
GRAM-NEGATIVE COCCI	1 (0.4%)		
TOTAL	**279 (100%)**	**153 (54.8 %)**	

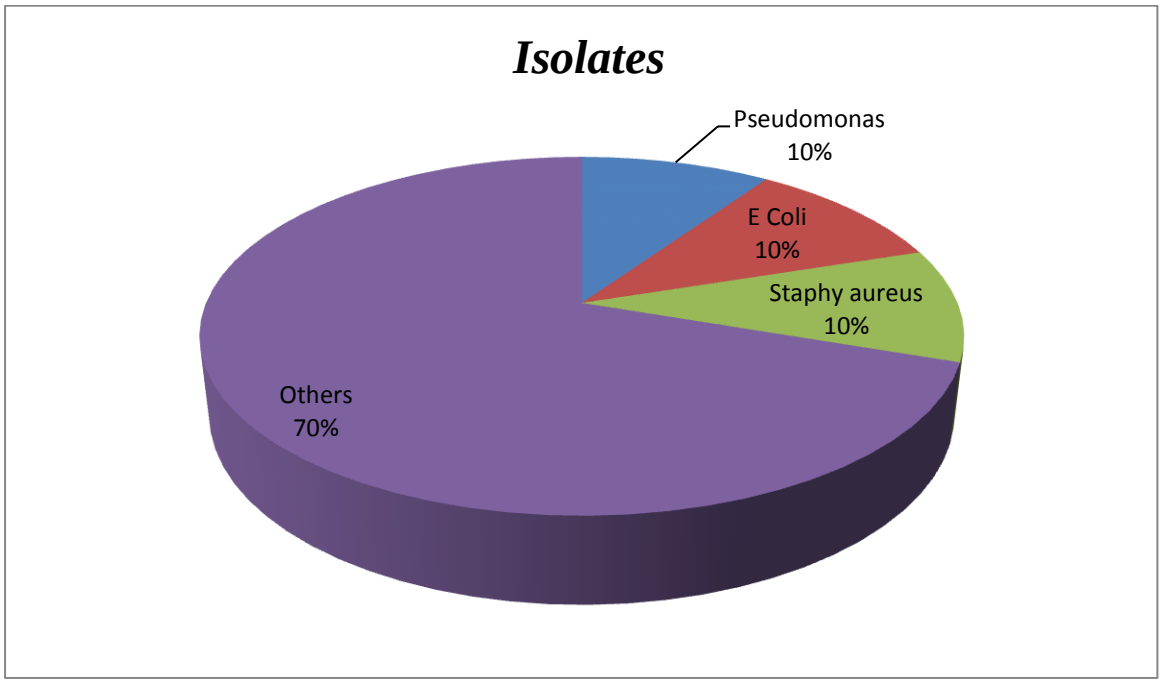
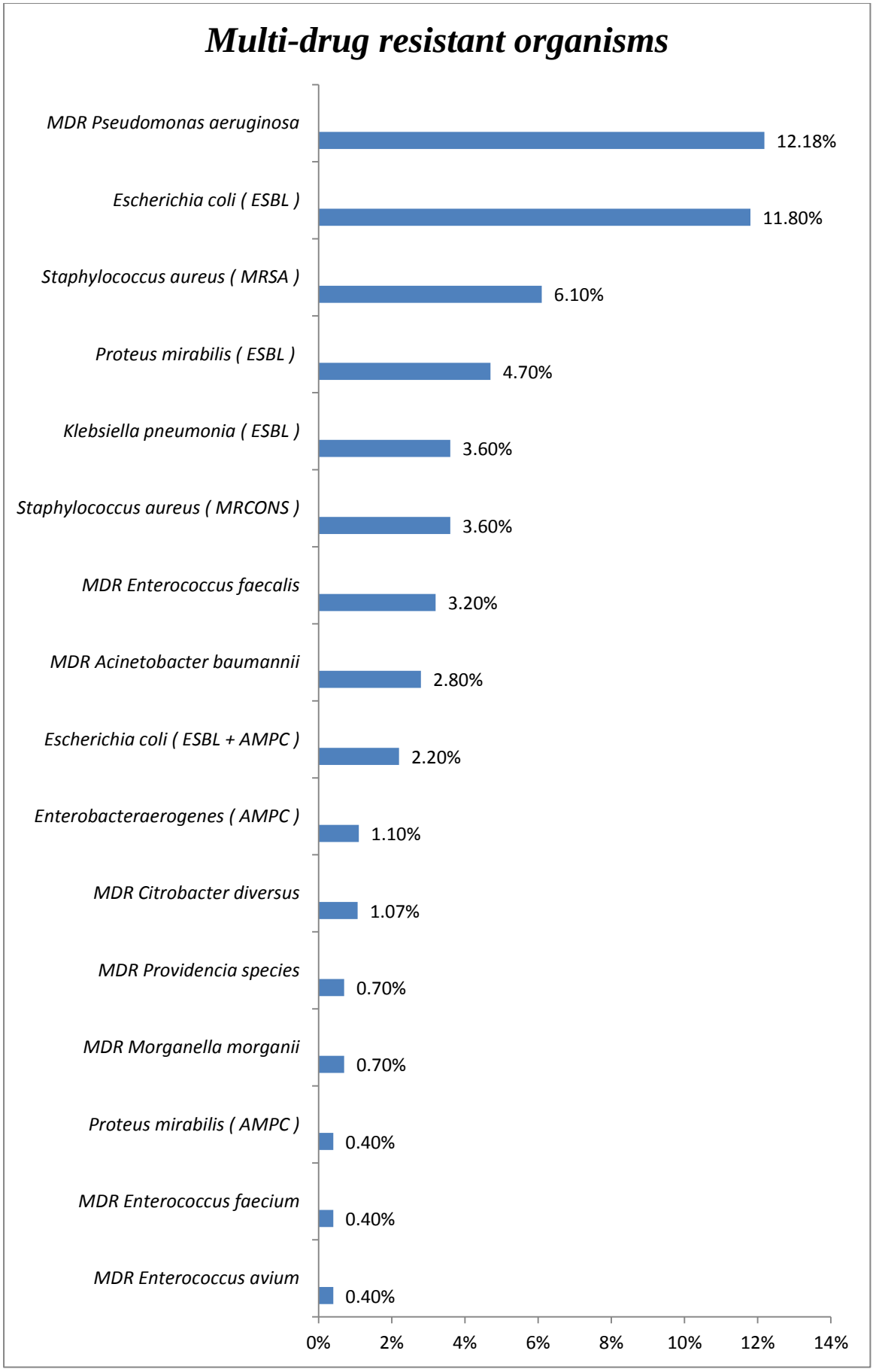


Table 9: List of Multidrug Resistant Organisms

MDROs	N	PERCENT
GRAM- POSITIVE COCCI		
Staphylococcus aureus (MRSA)	17	6.1 %
Staphylococcus aureus (MRCONS)	10	3.6 %
MDR Enterococcus avium	1	0.4 %
MDR Enterococcus faecalis	9	3.2 %
MDR Enterococcus faecium	1	0.4 %
GRAM-NEGATIVE RODS		
Enterobacter aerogenes (AMPC)	3	1.1 %
Escherichia coli (ESBL)	33	11.8 %
Escherichia coli (ESBL + AMPC)	6	2.2 %
Klebsiella pneumonia (ESBL)	10	3.6 %
Proteus mirabilis (ESBL)	13	4.7 %
Proteus mirabilis (AMPC)	1	0.4 %
MDR Acinetobacter baumannii	8	2.8 %
MDR Citrobacter diversus	3	1.07 %
MDR Morganella morganii	2	0.7 %
MDR Pseudomonas aeruginosa	34	12.18 %
MDR Providencia species	2	0.7 %
TOTAL	153	54.9 %


Multi-drug resistant organisms
MDR Pseudomonas aeruginosa
12.18%
Escherichia coli (ESBL)
11.80%
Staphylococcus aureus (MRSA)
6.10%
Proteus mirabilis (ESBL)
4.70%
Klebsiella pneumonia (ESBL)
3.60%
Staphylococcus aureus (MRCONS)
3.60%
MDR Enterococcus faecalis
3.20%
MDR Acinetobacter baumannii
2.80%
Escherichia coli (ESBL + AMPC)
2.20%
Enterobacteraerogenes (AMPC)
1.10%
MDR Citrobacter diversus
1.07%
MDR Providencia species
0.70%
MDR Morganella morganii
0.70%
Proteus mirabilis (AMPC)
0.40%
MDR Enterococcus faecium
0.40%
MDR Enterococcus avium
0.40%
0%
2%
4%
6%
8%
10%
12%
14%

MDRO vs NON-MDRO INFECTED ULCERATIONS:

The factors associated with MDRO infections were analysed. The test variables were compared using Chi-square test for qualitative variables and Student's test for quantitative variables. The variables for which the association was statistically significant ($p< 0.1$) were introduced in a logistic model to explain the presence of MDRO.

Results of the univariate analysis showed , poor glycaemic control, previous hospitalisation, previous history of amputation, previous antibiotic usage, size of ulcer, necrotic ulcer, recurrent ulcers, higher grade of ulcer,presence of osteomyelitis, presence of retinopathy, peripheral vascular disease, neuropathy and polymicrobial culture, were significantly associated with MDRO infected foot ulcers.

However logistic regression results indicated that only two factors significantly increased the chances of acquiring MDRO infection; recurrent ulcer (OR = 3.39, $p < 0.05$, 95 % CI = [1.081 – 10.664]), Higher grade of ulcer (OR = 13.44, $p < 0.001$, 95 % CI = [3.595 – 50.278]).

The association of factors like age and sex of the patient, socio-economic status, type and duration of diabetes, presence of nephropathy, hypertension, smoking, alcohol, site and duration of the ulcer with MDRO infected ulcers were statistically insignificant.

Table 10: MDRO versus NON-MDRO

VARIABLE	NON MDRO	MDRO	TOTAL	X^2	P VALUE
AGE					
< 40	3 (60 %)	2 (40 %)	5 (100 %)		
41 – 50	8 (50 %)	8 (50 %)	16 (100 %)		
51 – 60	14 (25.5 %)	41 (74.5 %)	55 (100 %)	6.373	0.272
61 – 70	22 (35.5 %)	40 (64.5 %)	62 (100 %)		
71 – 80	4 (40 %)	6 (60 %)	10 (100 %)		
81 – 90	0 (0 %)	2 (100 %)	2 (100 %)		
SEX					
Male	35 (31.2 %)	77 (68.8 %)	112 (100 %)	1.490	0.222
Female	16 (42.1 %)	22 (57.9 %)	38 (100)		
SOCIO ECO-STATUS					
Class I	14 (35.9 %)	25 (64.1 %)	39 (100 %)		
Class II	23 (34.8 %)	43 (65.2 %)	66 (100 %)		
Class III	12 (30.8 %)	27 (69.2 %)	39 (100 %)	0.266	0.966
Class IV	2 (33.3 %)	4 (66.7 %)	6 (100 %)		
Class V	0 (0 %)	0 (0 %)	0 (0 %)		
TYPE OF DIABETES					
I	3 (50 %)	3 (50 %)	6 (100 %)	0.713	0.398
II	48 (33.3 %)	96 (66.7 %)	144 (100 %)		
DEPTH OF ULCER					
Superficial	26 (28.3 %)	66 (71.7 %)	92 (100 %)		
Deep	25 (43.1 %)	33 (56.9 %)	58 (100 %)	3.492	0.062
NATURE OF ULCER					
Non necrotic	42 (53.8 %)	36 (46.2 %)	78 (100%)	28.52	0.000
Necrotic	9 (12.5 %)	63 (87.5 %)	72 (100 %)		
RECURRENCE					
Non recurrent	42 (53.2 %)	37 (46.8 %)	79 (100 %)		
Recurrent	9 (12.7 %)	62 (87.3 %)	71 (100 %)	27.31	0.000

VARIABLE	NON MDRO	MDRO	TOTAL	X^2	P VALUE
GRADE OF ULCER					
Class I	15 (88.2 %)	2 (11.8 %)	17 (100 %)		
Class II	26 (65 %)	14 (35 %)	40 (100 %)		
Class III	3 (6.7 %)	42 (93.3 %)	45 (100 %)	62.83	0.000
Class IV	6 (17.1 %)	29 (82.9 %)	35 (100 %)		
Class V	1 (7.7 %)	12 (92.3 %)	13 (100 %)		
RETINOPATHY					
Absent	44 (38.9 %)	69 (61.1 %)	113 (100 %)	4.978	0.026
Present	7 (18.9 %)	30 (81.1 %)	37 (100 %)		
NEPHROPATHY					
Absent	29 (37.7 %)	48 (62.3 %)	77 (100 %)	0.946	0.331
Present	22 (30.1 %)	51 (69.9 %)	73 (100 %)		
OSTEOMYELITIS					
Absent	43 (43.4 %)	56 (56.6 %)	99 (100 %)	11.549	0.001
Present	8 (15.7 %)	43 (84.3 %)	51 (100 %)		
ARTERIOPATHY					
Absent	38 (48.1 %)	41 (51.9 %)	79 (100 %)	14.789	0.000
Present	13 (18.3 %)	58 (81.7 %)	71 (100 %)		
NEUROPATHY					
Absent	20 (58.8 %)	14 (41.2 %)	34 (100 %)	12.0	0.001
Present	31 (26.7 %)	85 (73.3 %)	116 (100 %)		
HYPERTENSION					
Absent	19 (32.8 %)	39 (67.2 %)	58 (100 %)	0.065	0.799
Present	32 (34.8 %)	60 (65.2 %)	92 (100 %)		
GLYCEMIC CONTROL (HBA_1C)					
6-7 %(GOOD)	17 (58.6 %)	12 (41.4 %)	29 (100 %)	18.84	0.000
7-8 % (FAIR)	23 (42.6 %)	31 (57.4 %)	54 (100 %)		
>8 % (POOR)	11 (16.4 %)	56 (83.6 %)	67 (100 %)		

VARIABLE	NON MDRO	MDRO	TOTAL	X^2	P VALUE
PREVIOUS ADMISSION					
Not hospitalized	32 (45.7 %)	38 (54.3 %)	70 (100 %)	8.026	0.005
Hospitalized	19 (23.8 %)	61 (76.2 %)	80 (100 %)		
SMOKING					
Non smoker	30 (40 %)	45 (60 %)	75 (100 %)	2.406	0.121
Smoker	21 (28 %)	54 (72 %)	75 (100 %)		
ALCOHOLIC					
Non- alcoholic	33 (37.5 %)	55 (62.5 %)	88 (100 %)	1.162	0.281
Alcoholic	18 (29 %)	44 (71 %)	62 (100 %)		
HISTORY OF AMPUTATION					
Absent	45 (38.1 %)	73 (61.9 %)	118 (100 %)	4.216	0.040
Present	6 (18.8 %)	26 (81.2 %)	32 (100 %)		
CULTURE					
Mono microbial	31 (50 %)	31 (50 %)	62 (100 %)	12.05	0.001
Poly microbial	20 (22.7 %)	68 (77.3 %)	88 (100 %)		
SITE					
Plantar	10 (62.5 %)	6 (37.5 %)	16 (100 %)		
Margins	8 (33.3 %)	16 (66.7 %)	24 (100 %)	7.831	0.251
Heel	14 (33.3 %)	28 (66.7 %)	42 (100 %)		
Inter digital	10 (31.2 %)	22 (68.8 %)	32 (100 %)		
Malleoli	5 (27.8 %)	13 (72.2 %)	18 (100 %)		
Leg	4 (25 %)	12 (75 %)	16 (100 %)		
Multiple areas	0 (0 %)	2 (100 %)	2 (100 %)		
DURATION OF DIABETES					
(Years Mean)	1.84	2.02		t=	
(SD)	(0.94)	(1.02)		1.032	0.30

VARIABLE	NON MDRO	MDRO	TOTAL	X^2	P VALUE
DURATION OF ULCER (Months Mean) (SD)	1.49 (0.73)	1.42 (0.77)		t = 0.50	0.61
SIZE OF THE ULCER (cm^2 mean) (SD)	2.47 0.80	2.91 0.97		t = 2.76	0.006

Table 11: Logistic regression : MDRO Vs NON-MDRO

	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Nature	.172	.730	.056	1	.814	1.188	.284	4.970
Recurrence	1.222	.584	4.382	1	.036	3.395	1.081	10.664
Grade	2.599	.673	14.910	1	.000	13.445	3.595	50.278
Retinopathy	.221	.631	.123	1	.726	1.247	.362	4.292
Osteomyelitis	-.260	.672	.150	1	.699	.771	.206	2.880
Pvd	.540	.537	1.013	1	.314	1.716	.600	4.911
Neuropathy	-.275	.675	.166	1	.684	.760	.202	2.854
hba1c	1.105	.631	3.062	1	.080	3.019	.876	10.403
Prev-hospital	.161	.608	.070	1	.791	1.175	.357	3.870
His.ofampuation	.630	.769	.672	1	.412	1.878	.416	8.481
Prevantibiotics	.267	.636	.176	1	.675	1.305	.376	4.537
Culture	.889	.523	2.884	1	.089	2.432	.872	6.783
Size	.293	.285	1.053	1	.305	1.340	.766	2.345
Age	-.005	.029	.029	1	.865	.995	.939	1.054
Constant	-3.418	2.054	2.767	1	.096	.033		

IMPACT OF MDROs :

The mean duration of hospital stay in MDRO infections was 15.36 days and that of non-MDRO infections was 8.88 days. The difference was statistically significant ($p< 0.001$).

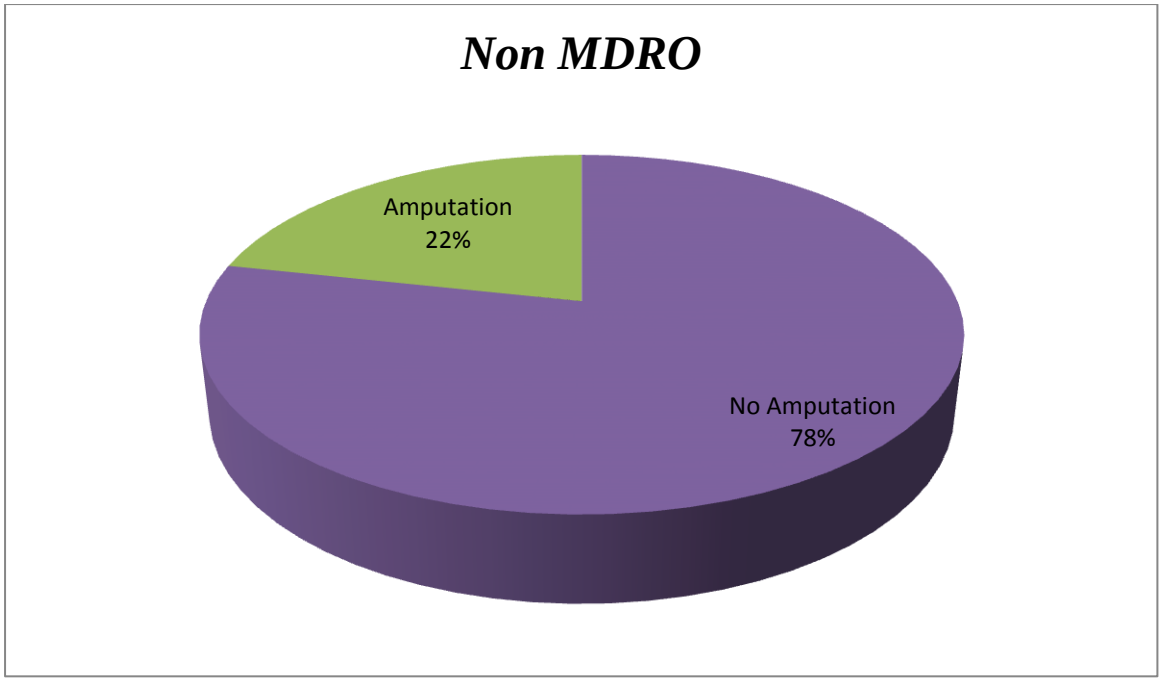
Table 12 : Mean duration of hospital stay :

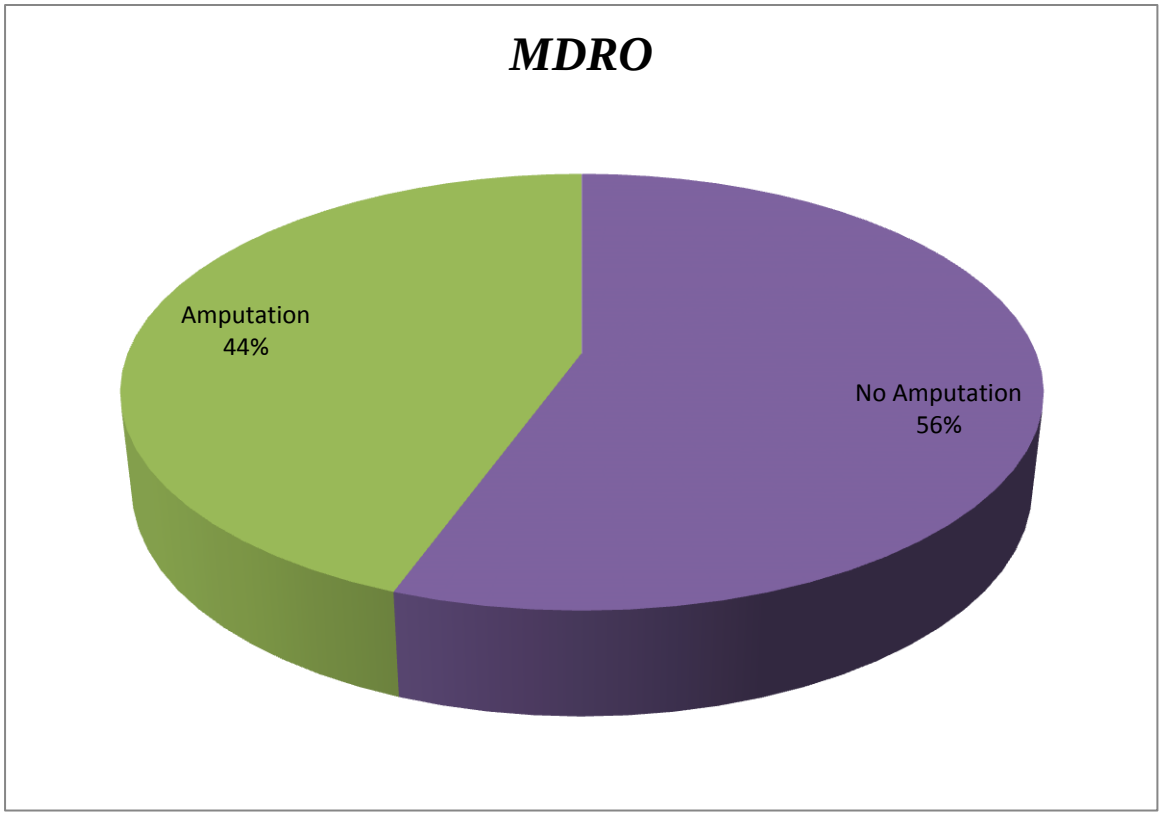
	MDRO	N	Mean	Std. Deviation	Std. Error Mean	t	P value
stay	Non MDRO	51	8.88	6.716	.940		
	MDRO	99	15.36	10.536	1.059	3.992	0.000

Presence of multi drug resistant organisms in the foot ulcers was associated with statistically significant increased frequency of amputations, both major and minor ($p < 0.01$). In the MDRO group 44.4 % of patients had some form of amputations, where as in non-MDRO group only 21.6 % of the patients had amputations.

Table 13 : MDROs & Amputations :

	NO AMPUTATION	AMPUTATION	TOTAL	X^2	P VALUE
NON MDRO	40 (78.4 %)	11 (21.6 %)	51 (100 %)	7.585	0.006
MDRO	55 (55.6 %)	44 (44.4 %)	99 (100 %)		


Non MDRO
Amputation
22%
No Amputation
78%


MDRO
Amputation
44%
No Amputation
56%

WOUND HEALING :

Based on the status of the ulcer at 10 weeks time the patients were grouped as healed and non-healed group. Healed group included the patients whose ulcers were completely healed and reduced in size. The rest were in the non-healed group. 60 patients were in healed group and 90 were in the non-healed group.

By univariate analysis, nature of ulcer, recurrent ulcer, grade of ulcer, underlying osteomyelitis, PVD, site of ulcer, culture, size of the ulcer, presence of nephropathy, neuropathy and the glycemic control were significantly ($p < 0.05$) associated with poor healing of the ulcer. Depth of the ulcer and presence of retinopathy had borderline ($p<0.1$) association with poor healing.

Table 14 : Healed Vs Non-Healed group :

VARIABLE	HEALED	NOT-HEALED	TOTAL	X^2	P VALUE
AGE					
< 40	2 (40 %)	3 (60 %)	5 (100 %)		
41 – 50	7 (43.8 %)	9 (56.2 %)	16 (100 %)		
51 – 60	18 (32.7 %)	37 (67.3 %)	55 (100 %)	3.744	0.587
61 – 70	28 (45.2 %)	34 (54.8 %)	62 (100 %)		
71 – 80	5 (50 %)	5 (50 %)	10 (100 %)		
81 – 90	0 (0 %)	2 (100 %)	2 (100 %)		
SEX					
Male	45 (40.2 %)	67 (59.8 %)	112 (100 %)	0.006	0.939
Female	15 (39.5 %)	23 (60.5 %)	38 (100)		

VARIABLE	HEALED	NOT-HEALED	TOTAL	X^2	P VALUE
SOCIO ECO-STATUS					
Class I	20 (51.3 %)	19 (48.7 %)	39 (100 %)		
Class II	22 (33.3 %)	44 (66.7 %)	66 (100 %)	5.34	0.148
Class III	14 (35.9 %)	25 (64.1 %)	39 (100 %)		
Class IV	4 (66.7 %)	2 (33.3 %)	6 (100 %)		
Class V	0 (0 %)	0 (0 %)	0 (0 %)		
TYPE OF DIABETES					
I	2 (33.3 %)	4 (66.7 %)	6 (100 %)	0.116	0.734
II	58 (40.3 %)	86 (59.7 %)	144 (100 %)		
DEPTH OF ULCER					
Superficial	36 (39.1 %)	56 (60.9 %)	92 (100 %)	0.075	0.062
Deep	24 (41.4 %)	34 (58.6 %)	58 (100 %)		
NATURE OF ULCER					
Non necrotic	49 (62.8 %)	29 (37.2 %)	78 (100%)	35.26	0.000
Necrotic	11 (15.3 %)	61 (84.7 %)	72 (100 %)		
RECURRENCE					
Non recurrent	42 (53.2 %)	37 (46.8 %)	79 (100 %)	12.05	0.001
Recurrent	18 (25.4 %)	53 (74.6 %)	71 (100 %)		
GRADE OF ULCER					
I	16 (94.1 %)	1 (5.9 %)	17 (100 %)		
II	26 (65 %)	14 (35 %)	40 (100 %)	53.21	0.000
III	14 (31.1 %)	31 (68.9 %)	45 (100 %)		
IV	4 (11.4 %)	31 (88.6 %)	35 (100 %)		
V	0 (0 %)	13 (100 %)	13 (100 %)		
RETINOPATHY					
Absent	50 (44.2 %)	63 (55.8 %)	113 (100 %)	3.44	0.063
Present	10 (27 %)	27 (73 %)	37 (100 %)		

VARIABLE	HEALED	NOT-HEALED	TOTAL	X^2	P VALUE
NEPHROPATHY Absent Present	 37 (48.1 %) 23 (31.5 %)	 40 (51.9 %) 50 (68.5 %)	 77 (100 %) 73 (100 %)	4.27	0.046
OSTEOMYELITIS Absent Present	 54 (54.5 %) 6 (11.8 %)	 45 (45.5 %) 45 (88.2 %)	 99 (100 %) 51 (100 %)	25.668	0.000
ARTERIOPATHY Absent Present	 45 (57.0 %) 15 (21.1 %)	 34 (43.0 %) 56 (78.9 %)	 79 (100 %) 71 (100 %)	20.008	0.000
NEUROPATHY Absent Present	 25 (73.5 %) 35 (30.2 %)	 9 (26.5 %) 81 (69.8 %)	 34 (100 %) 116 (100 %)	20.59	0.000
HYPERTENSION Absent Present	 22 (37.9 %) 38 (41.3 %)	 36 (62.1 %) 54 (58.7 %)	 58 (100 %) 92 (100 %)	0.169	0.681
GLYCEMIC CONTROL (HBA1C) 6-7 %(GOOD) 7-8 % (FAIR) >8 % (POOR)	 21 (72.4 %) 31 (57.4 %) 8 (11.9 %)	 8 (27.6 %) 23 (42.6 %) 59 (88.1 %)	 29 (100 %) 54 (100 %) 67 (100 %)	41.49	0.000
PREVIOUS HOSPITALIZATION Not Hospitalized Hospitalized	 33 (47.1 %) 27 (33.8 %)	 37 (52.9 %) 53 (66.2 %)	 70 (100 %) 80 (100 %)	2.79	0.095
SMOKING Non smoker Smoker	 34 (45.3 %) 26 (34.7 %)	 41 (54.7 %) 49 (65.3 %)	 75 (100 %) 75 (100 %)	1.778	0.182

VARIABLE	HEALED	NOT-HEALED	TOTAL	X^2	P VALUE
H/0 AMPUTATION Absent Present	 49 (41.5 %) 11 (34.4 %)	 69 (58.5 %) 21 (65.6 %)	 118 (100%) 32 (100 %)	0.536	0.464
ALCOHOLIC Non- alcoholic Alcoholic	 38 (43.2 %) 22 (35.5 %)	 50 (56.8 %) 40 (64.5 %)	 88 (100 %) 62 (100 %)	0.898	0.343
SITE Plantar Margins Heel Inter digital Malleoli Leg Multiple areas	 10 (62.5 %) 9 (37.5 %) 18 (42.9 %) 6 (18.8 %) 12 (66.7 %) 4 (25 %) 1 (5 0 %)	 6 (37.5 %) 15 (62.5 %) 24 (57.1 %) 26 (81.2 %) 6 (33.3 %) 12 (75 %) 1 (50 %)	 16 (100 %) 24 (100 %) 42 (100 %) 32 (100 %) 18 (100 %) 16 (100 %) 2 (100 %)	16.51	0.011
PREVIOUS ANTIBOTIC USAGE Absent Present	 38 (44.2 %) 22 (34.4 %)	 48 (55.8 %) 42 (65.6 %)	 86 (100 %) 64 (100 %)	1.472	0.225
CULTURE Mono microbial Poly microbial	 35 (56.5 %) 25 (28.4 %)	 27 (43.5 %) 63 (71.6 %)	 62 (100 %) 88 (100 %)	11.91	0.001
DURATION OF DIABETES (Years Mean) (SD)	 1.83 (0. 886)	 2.04 (1.059)		t= 1.275	0.204
DURATION OF ULCER (Months Mean) (SD)	 1.52 (0.770)	 1.40 (0.747)		t = 0.926	0.356

VARIABLE	HEALED	NOT-HEALED	TOTAL	X^2	P VALUE
SIZE OF THE ULCER (CM^2 Mean) (SD)	2.5 0.893	2.93 0.934		t = 2.834	0.005
DRUG RESISTANCE MDRO NON MDRO	24 (24.2 %) 36 (70.6 %)	75 (75.8 %) 15 (29.4 %)	99 (100 %) 51 (100 %)	30.12	0.000

Table 15 : Logistic regression:

		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1[a]	ageno	-.060	.033	3.228	1	.072	.942	.882	1.005
	size	.297	.339	.768	1	.381	1.346	.693	2.617
	depth(1)	-.157	.673	.054	1	.816	.855	.228	3.199
	nature(1)	.775	.745	1.081	1	.298	2.170	.504	9.353
	recurrence(1)	-.996	.702	2.016	1	.156	.369	.093	1.461
	retinopathy(1)	-.780	.717	1.182	1	.277	.459	.112	1.870
	nephropathy(1)	1.474	.648	5.174	1	.023	4.369	1.226	15.564
	osteomyelitis(1)	2.114	.788	7.202	1	.007	8.280	1.768	38.766
	pvd(1)	2.063	.697	8.766	1	.003	7.872	2.009	30.849
	neuropathy(1)	.391	.727	.290	1	.590	1.479	.356	6.145
	site			10.174	6	.118			
	site(1)	-.842	1.166	.522	1	.470	.431	.044	4.231
	site(2)	-1.233	1.104	1.246	1	.264	.292	.033	2.540
	site(3)	.800	1.164	.472	1	.492	2.226	.227	21.819
	site(4)	-2.612	1.261	4.290	1	.038	.073	.006	.869
	site(5)	-.638	1.379	.214	1	.644	.528	.035	7.883
	site(6)	-2.416	2.353	1.054	1	.304	.089	.001	8.987
	culture(1)	.927	.597	2.411	1	.120	2.527	.784	8.147
	mdro(1)	1.109	.754	2.163	1	.141	3.031	.691	13.283
	hba1c1	1.795	.806	4.959	1	.026	6.020	1.240	29.226
	grade1	1.413	.796	3.150	1	.076	4.107	.863	19.549
	Constant	-1.638	2.330	.494	1	.482	.194		

However logistic regression showed only the following factors, significantly delayed the chances of wound healing : PVD (OR = 7.872, $p < 0.01$, 95 % CI = [2.009 – 30.849]), Osteomyelitis (OR = 8.280, $p<0.01$, 95 % CI = [1.768 – 38.766]), Presence of nephropathy (OR = 4.36, $p < 0.05$, 95 % CI = [1.226 – 15.564]), Inter-digital / digital ulcer (OR = 0.073, $p < 0.05$, 95 % CI = [0.006 – 0.869]), HbA1c (OR = 6.020, $p < 0.05$, 95 % CI = [1.240 – 29.226]), Age (OR = 0.942, $p <0.1$, 95 % CI = [0.882 – 1.005]), Grade of ulcer (OR = 4.10, $p <0.1$, 95 % CI = [0.863 – 19.549]) .

MDR infected ulcers had no impact on wound healing. Other factors like socio-economic status, type of diabetes, smoking, alcohol, duration of ulcer had no role in determining the wound healing.

DISCUSSION

This study presents a comprehensive clinical and microbiological profile of infected diabetic foot ulcers, especially in relation to multidrug resistant organisms. As already discussed India is the diabetic capital of the world[2], and South India is the diabetic capital of India. With some reports of nearly 20% of hospital admissions being infected diabetic foot ulcers [11] and with the growing global problem of multidrug resistant organisms[68], we made an effort to study the role of multidrug resistant organisms in relation to diabetic foot ulcers, here at Coimbatore.

In our study the foot ulcers were more prevalent in the fifth and sixth decade of life. The average age of the patients with foot ulcer was 58.21 ± 9.3 years, which is similar to the age prevalence described in other Indian studies [12,69,70,71] . The foot ulcers were more common in male than female, which may be due to higher level of manual work and outdoor activity among male when compared to females. Similar gender preponderance was observed in studies conducted in India [12,72].

In our study, most of the patients with ulcer had diabetes of less than 5 years duration. This observation was in contrast with other studies conducted in the country [12,72] which showed more ulcers occurring in patients having diabetes for longer duration. This might well reflect the profile of all diabetic patients visiting the hospital, and will need an in depth examination to ascertain this.

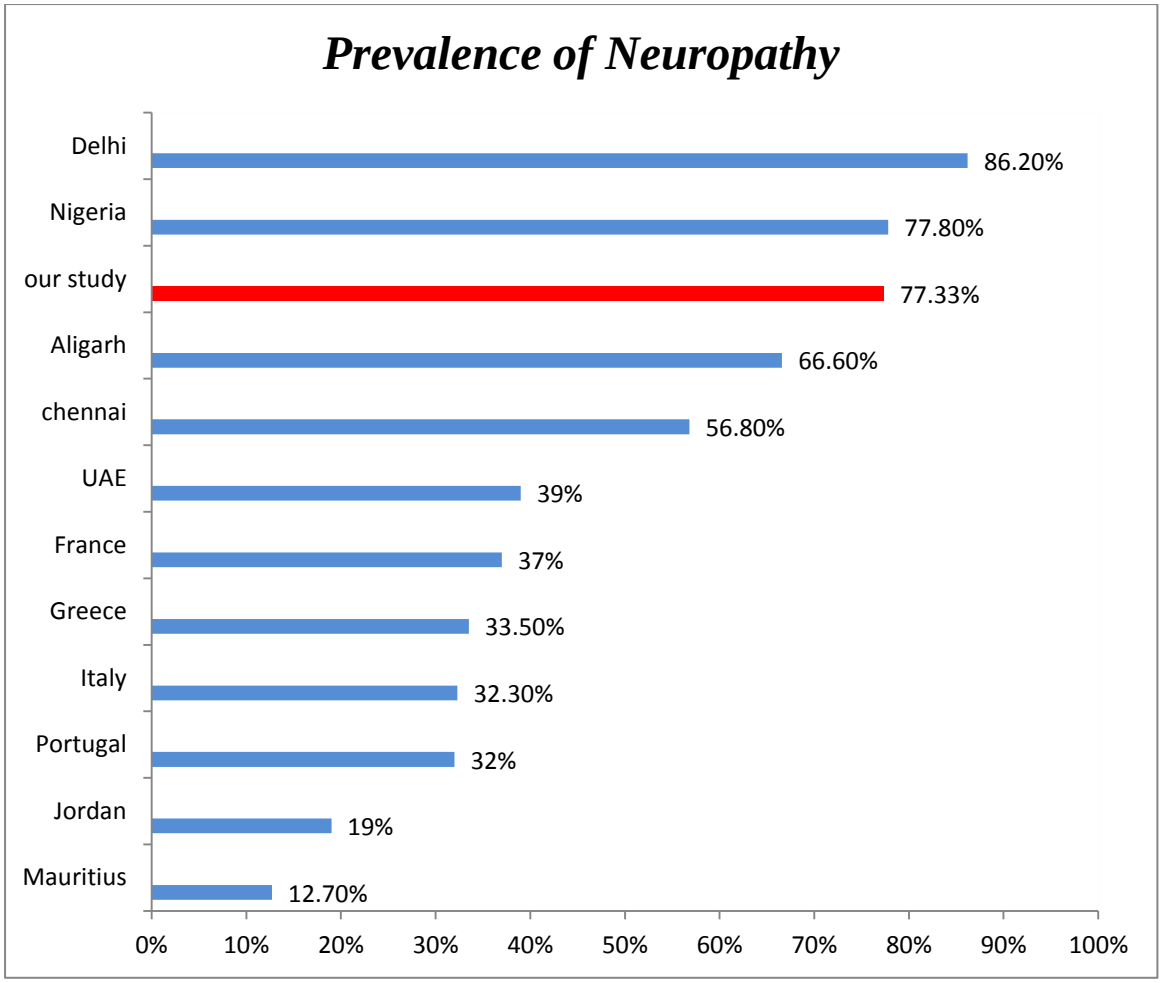
Most of the patients (68%) had ulcers of less than 1 month duration which is similar to the observations from a north Indian study[72]. But according to another north Indian study[12] most

ulcers presented to hospital after 3 months. An early presentation is often due to the fact that ulcers with acute onset often have systemic symptoms which bring the patients to the hospital, while in chronic ulcers the symptoms are mild and localised.

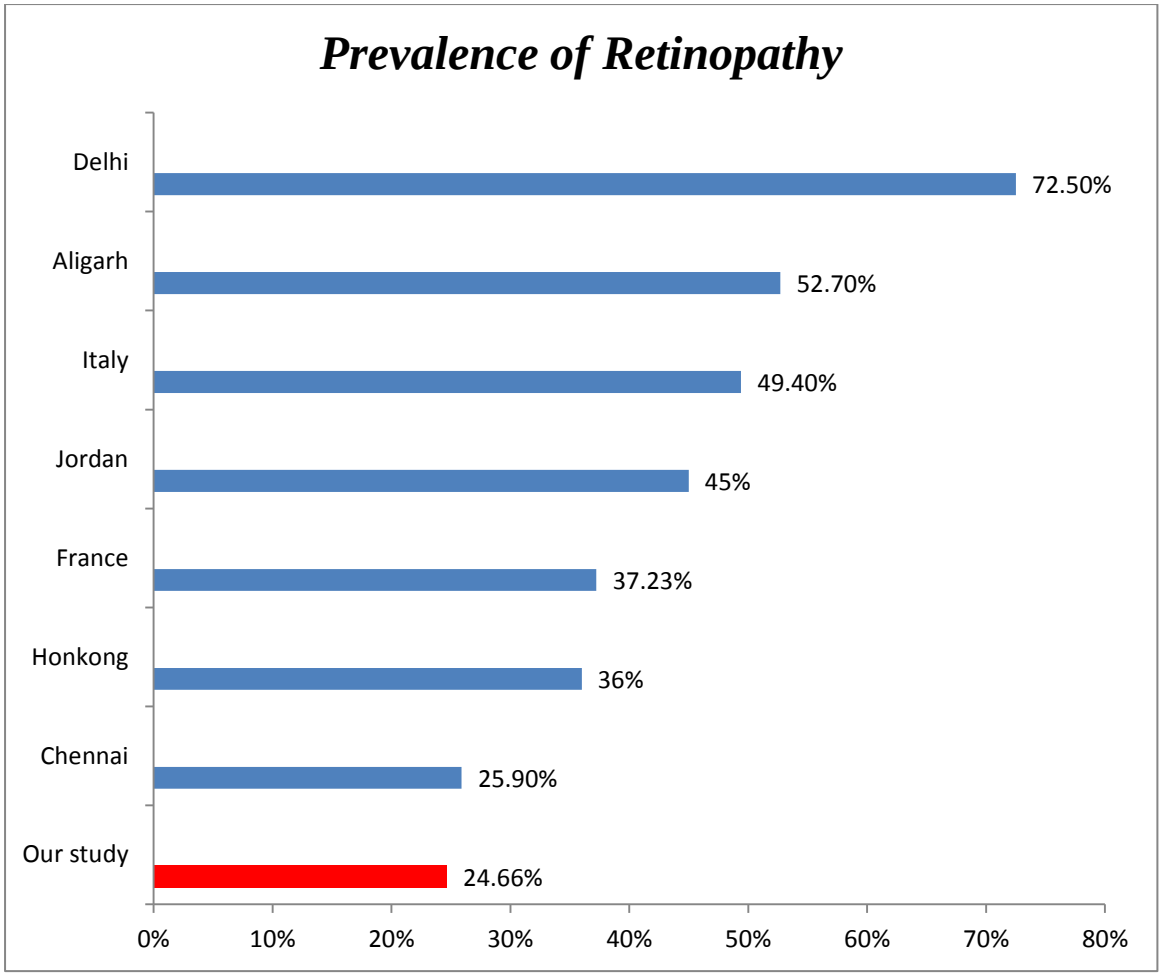
Comparable with the literature [12,72], most of the patients in the present study had poor glycaemic control. Poor glycaemic control is associated with greater degree of microvascular complications.

Majority of the patients in our study had higher grade of ulcers (Wagners grade III or worse) similar to the other north Indian studies [12,72]. The reason for presentation with higher grade could be because of lack of structured health care delivery in the country, attempted self medication and trust in traditional healers[73].

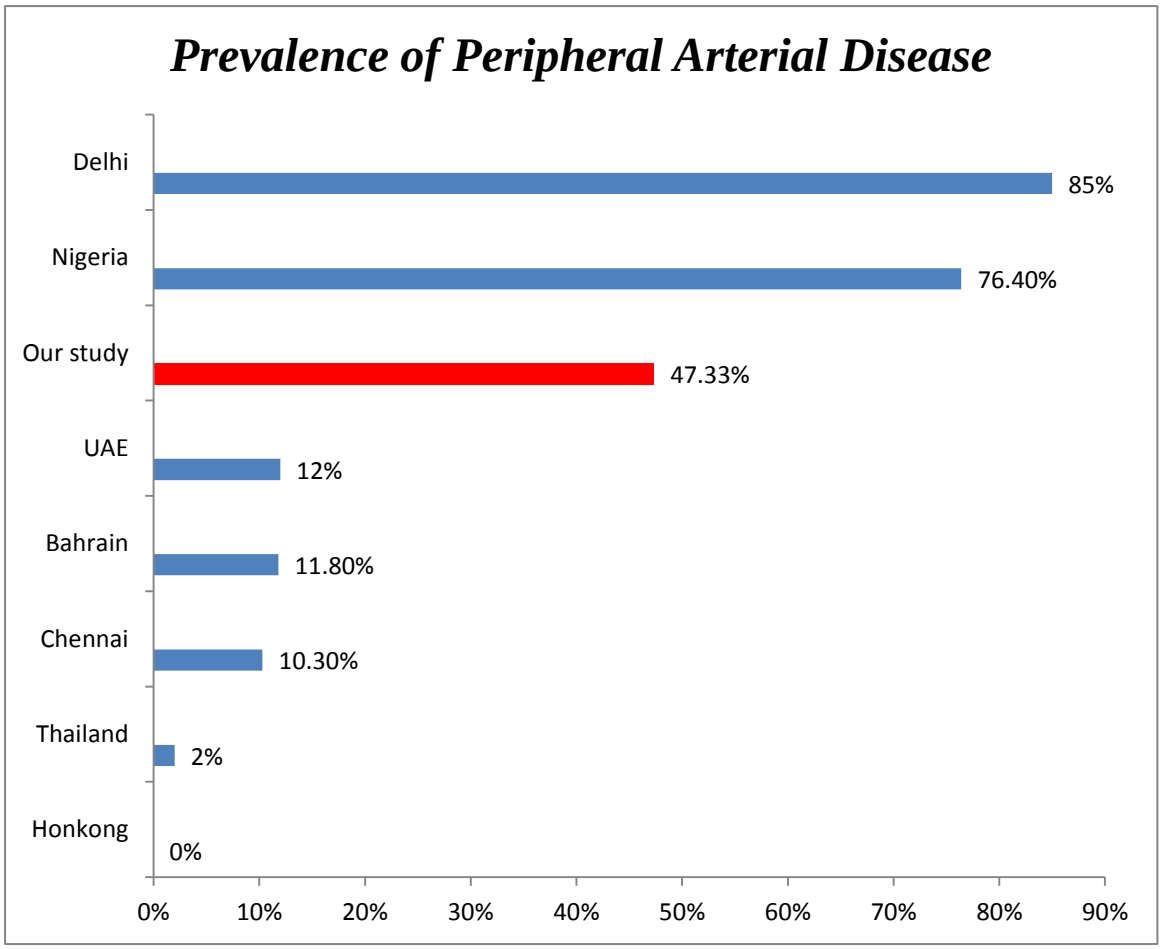
In the present study the neuropathy was seen in 77.33% of the diabetic foot ulcer patients. The other studies reported from India [12,72,11] showed a similar high prevalence (86.2% , 66.6%, and 56.8 % respectively).Whereas studies done in other countries showed a varied prevalence. A Nigerian study [10] showed prevalence of 77.8%. An UAE [74]study showed 39% prevalence. Mauritius study [76] and Jordan study[77] showed a prevalence of 12.7% and 19% respectively.European studies[75,78,79]have a shown a prevalence ranging from 32 to 33.5% . This marked variation in the prevalence may be due to varied methods used for diagnosing neuropathy(monofilament testing ,biothesiometer, scoring systems). However, this does show a higher prevalence in Indian population. This could be because of patient's ignorance and poor glycemic control.

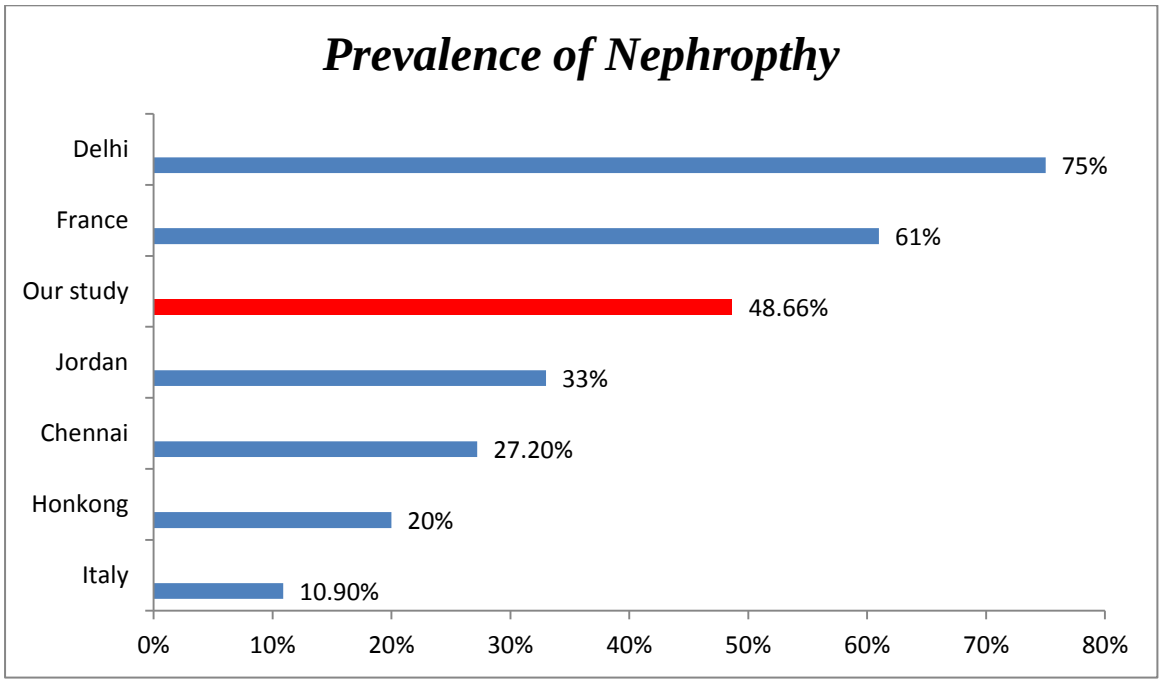


In our study, the prevalence of retinopathy was 24.66%. This observation was similar to another south Indian study[11] which showed a prevalence of 25.9%. But the studies conducted in northern Indian [72,12] showed a higher prevalence – 52.7% and 72.5% respectively. Thus the prevalence is lower in south India when compared to other countries. This is in line with the overall lower prevalence of diabetic retinopathy in southern India[80]. Prevalence of retinopathy among foot ulcer patients in studies from Jordan[77], France [81], Hong Kong [82], and Italy [83] were 45%, 37.23%, 36%, and 49.4% respectively.



Peripheral arterial disease was observed in 47.33% of our study group. The other previously reported studies showed highly variable results. A north indian study[12] showed a very high prevalence of 85%. On the other hand the study from south India [11] showed a prevalence of 10.3%. Similarly the prevalence varied between countries also, Nigeria[84] – 76.4%, Bahrain[85] – 11.8%, UAE[74] – 12%, Thailand [86]– 2%, Honkong[82] – 0%.


Prevalence of Peripheral Arterial Disease
Delhi
Nigeria
Our study
UAE
Bahrain
Chennai
Thailand
Honkong
85%
76.40%
47.33%
12%
11.80%
10.30%
2%
0%
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%

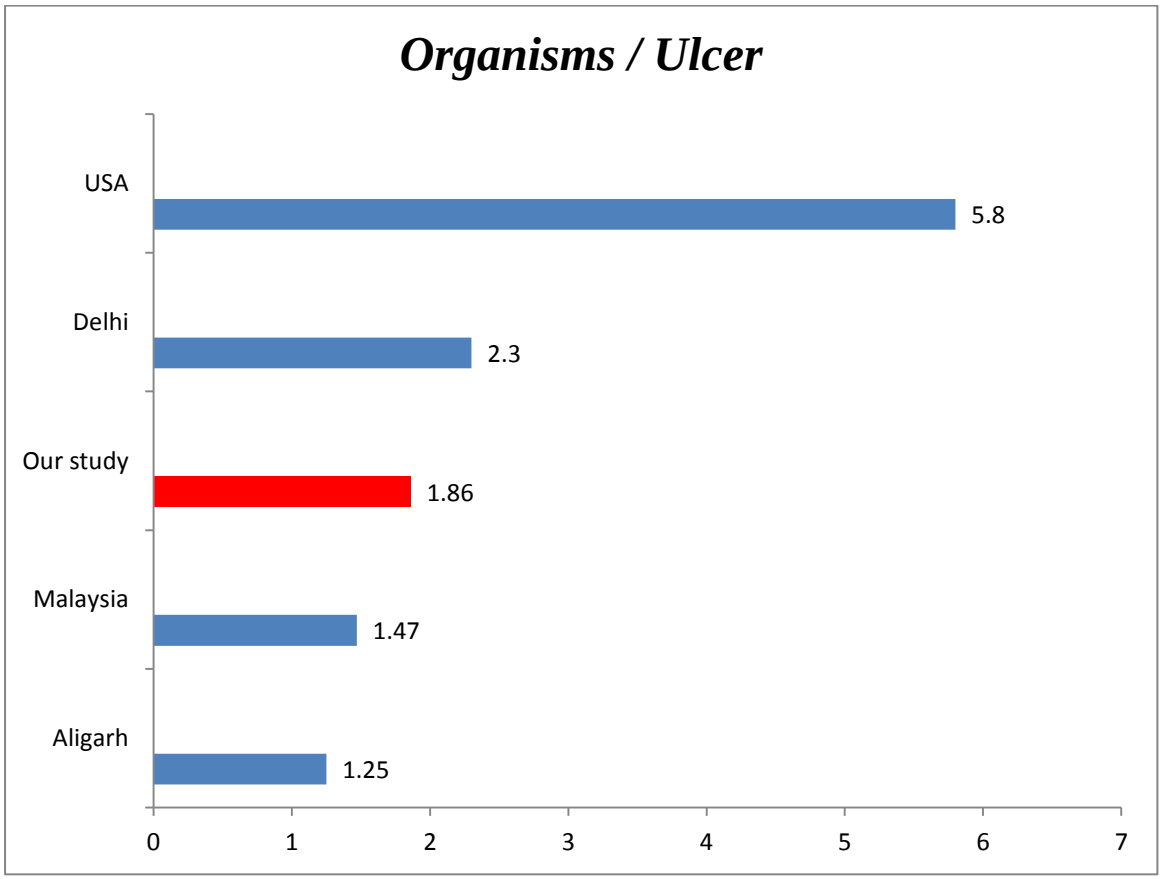

Prevalence of Nephropthy
Delhi
France
Our study
Jordan
Chennai
Honkong
Italy
75%
61%
48.66%
33%
27.20%
20%
10.90%
0%
10%
20%
30%
40%
50%
60%
70%
80%

The prevalence of nephropathy was 48.66% in our study. The north indian study[12] showed a high prevalence(75%). A study from south India showed 27.2 %[11]. Studies from other countries also showed a lower prevalence, Jordan[77] – 33%, Honkong[82] – 20%, Italy[83] – 10.9%.

The bacteriological evaluation of diabetic foot ulcer from our study showed that the gram negative organisms were found have a higher occurrence than gram positive organisms in the ratio 2.3 :1. Some of the other Indian studies[12,72,11]also showed a higher occurrence of gram negative organisms with ratios of 1.5 : 1[12], and 1.3: 1[72]. Comparatively our study did show a higher ratio. A study from Malaysia[64] also showed the same. However, most of the western literature showed a predominance of gram positive organisms as supposed to gram negative organisms [22,50,81,87,88]. This could be partly due to differences in the causative organisms occurring over time, geographical variations, or the types and severity of infection included in the studies [89].

Diabetic foot infection are usually polymicrobial in nature which is well documented in literature. In our study, 58.66 % of ulcers had polymicrobial culture. Similar observations were found in other Indian studies(Gadepalli et al[12], Mohammed zubair et al[72], Shankar et al[11], Vishwanathan et al[65])and western studies (Dian M Citron et al[89], Wright-Poscoe[90] et al.). There are however a few studies (Dhanasekarenet al[91] and Sajeed et al[64])which showed more patients with monomicrobial culture. Polymicrobial infection, to a certain extent, may be due to prior treatment history of the patients studied, as reported earlier [39,52,92].

In our study, the rate of isolation of organism per ulcer was 1.86 while the other two indianstudies(Mohammed et al [72], Gadepalli [12]) showed a rate of 1.25 and 2.3 organisms per ulcer. A study from Malaysian reported[64] 1.47 org / lesion. A study from US[38] by Gerding et al, showed a very high rate of 5.8 organisms recovered from the ulcer.

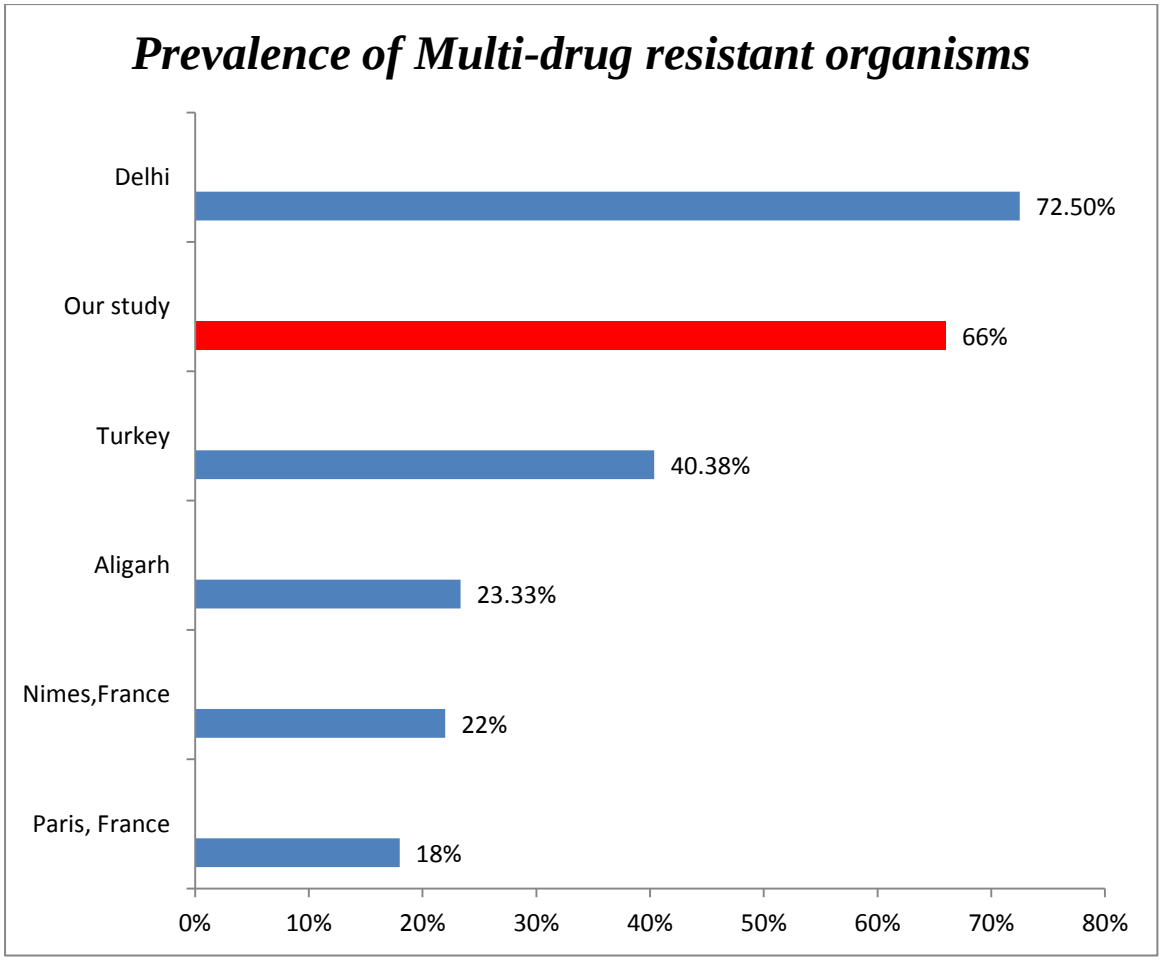


The commonest organism isolated in our study was Escherechia coli followed by Staphylococcus aureus, Pseudomonas and Klebsiella pneumoniae. This is similar to the observations from a south indian study[65]. Another south Indian study[11], showed Pseudomonas aeruginosa as the commonest isolate. But most of the other studies from India[72,12] and other countries[89,64,81]showed Staphylococcus aureus as the commonest isoloate from diabetic foot ulcers.

In our study, the third predominant organism was Pseudomonas (16.5 %). Two other studies[81,11] also showed higher recovery of Pseudomonas. The gram negative bacilli, Pseudomonas, which were once considered as normal flora of the skin, may cause severe tissue damage in diabetics and should never be regarded as insignificant in diabetic foot ulcers[93].

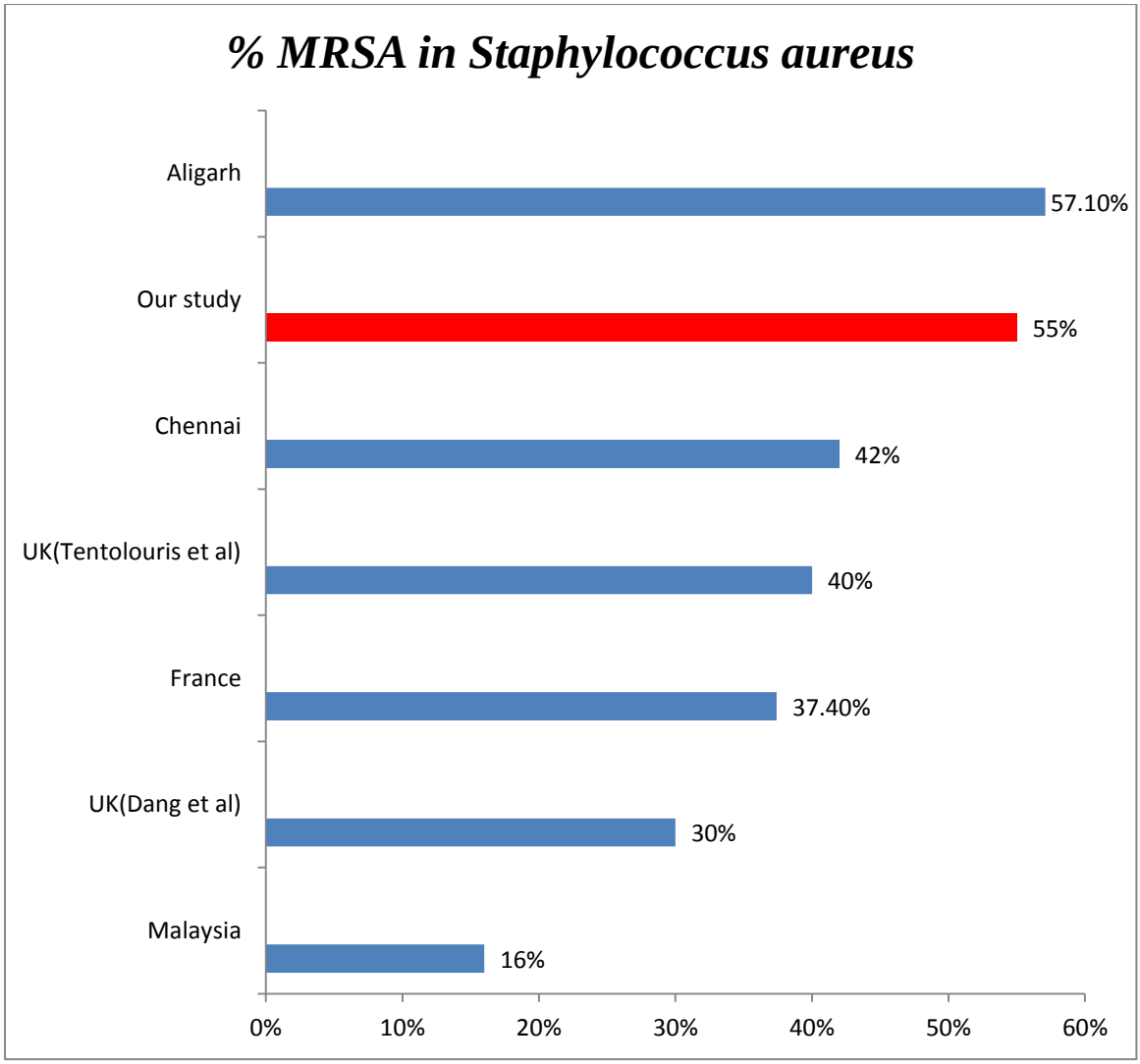
In our study 66 % of the ulcers grew multi-drug resistant organisms (MDRO) and 54.8% of isolated organisms were multi drug resistant. Many different definitions for multi-drug resistant organisms were used in medical literature. Due to the lack of uniform definition for MDROs the overall prevalence of MDRO, as seen in the literature, could not be studied. European centre for disease prevention and control has arrived at a definition for MDROs and has laid up specific criteria for categorising an organism as MDRO[67].

Apart from the multi drug resistant organisms like MRSA, ESBL, VRE which were extensively studied in literature, other groups of organisms like MDR Psudomonas, Acinetobacter, Enterococcus, Enterobactereciae etc were also identified in our study. The higher prevalence of multidrug resistant organisms was also observed in another north Indian study (Gadepalliet al[12]). The higher degree of antibiotic resistance in tertiary care hospitals, could be because, with widespread usage of broad spectrum antibiotics, there occurs selective survival of drug resistant organisms. Western literature (Richard et al [81]– 22 % of isolate ,Kandemir O et al [94]- 40.38 %) showed a lower prevalence of MDRO when compared to Indian literature, perhaps a reflection of higher antibiotic use and abuse. The increasing occurrence of MDROs is disconcerting because, infection with these organisms limits the choice of antibiotic treatment and may lead to a worse outcome.

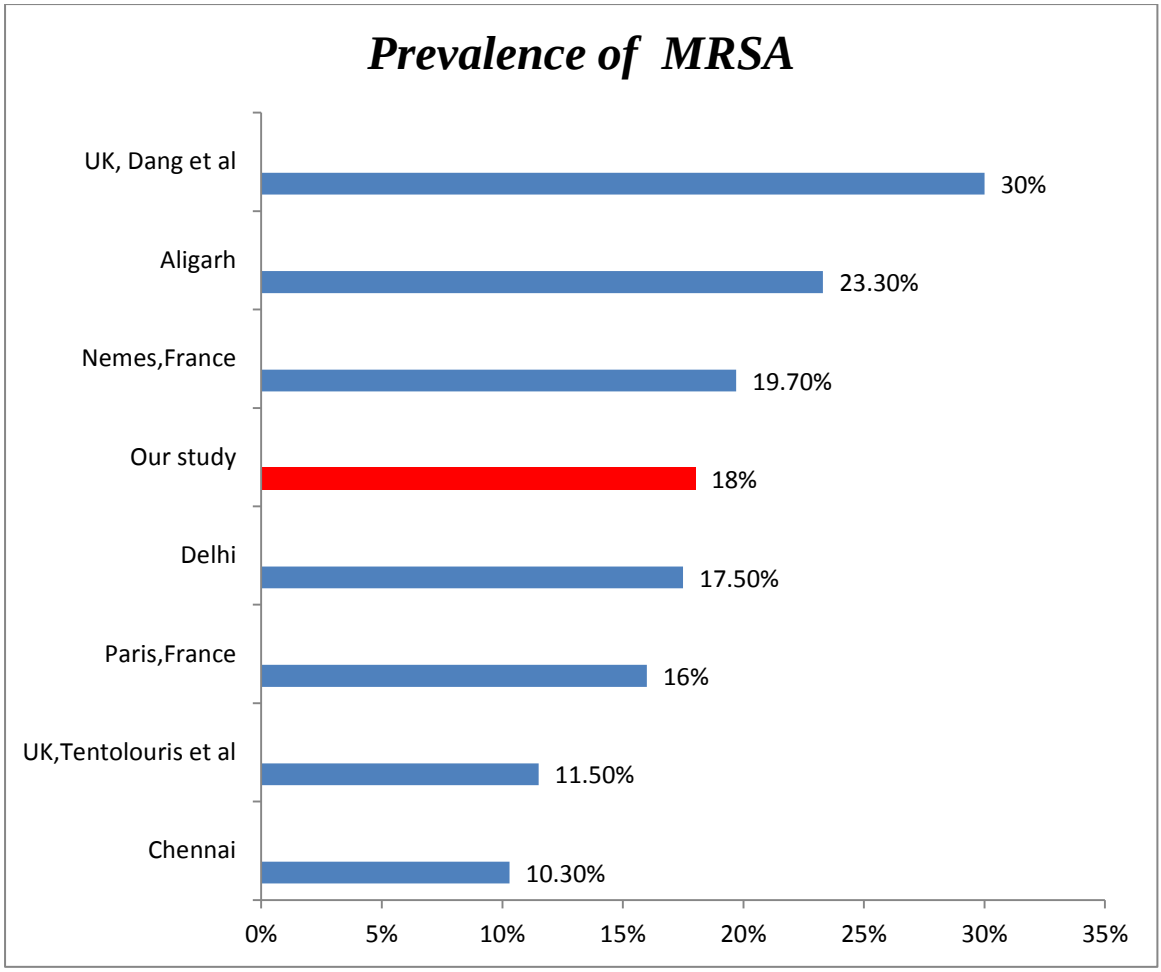


Our study showed that 75% of all MDROs isolated were gram negative organisms. It is a fact that higher degree of antibiotic resistance is observed in gram negative organisms when compared to gram positive organisms. This is because gram negative organisms have a unique outer membrane which does not allow certain antibiotics to penetrate.

55% (27 out of 49 isolates) of Staphylococcus aureus isolated from our study were methicillin resistant. A similar observation was found in the north Indian study [72], which showed 57.1%, and in the south Indian study alluded to earlier, it was 42% [11]. But studies from other countries showed a lower percentage. A study done in France showed (Richard et al[81]) 37.4%. 2 studies done in UK (Tentalouris et al [50], Dang C N et al[22]) showed 40% and 30% respectively. A much lower percentage (16%) was observed in a Malaysian study[64].



MRSA was seen in 18% of the patients in our study. These results were similar to the previous Indian studies. 17.5% and 23.3% were seen respectively in the two north Indian studies (Gadepalli et al [12]) & (MohammedZubair et al [72]). A study done in South India (Shankar et al [11]) had an occurrence of 10.3%. The studies from the west , France (Richard et al[81], Hartemann et al[60]), UK (Dang C N et al [22,]Tentalorius et al[50]) showed 19.7%, 16%, 30%, 11.5% respectively .



20.4 % of isolated staphylococcus aureus were Methicillin resistant and coagulase negative (MRCONS), the reports of which in relation to diabetic ulcers were not looked at in the previous studies. In our study we also identified other multi drug resistant gram positive organisms such as MDR Enterococcus avium, Enterococcus faecalis, and Enterococcus faecium, in relation to diabetic foot ulcers (using the guidelines proposed by European centre for disease prevention and control[67]). These were not observed in previous studies.

With regard to the gram negative organisms in our study, E.coli showed greater antibiotic resistance, followed by Pseudomonas aeruginosa. 78 % of isolated E.coli and 74 % of isolated Pseudomonas were multi-drug resistant.

In the last two decades, we have seen the emergence of extended spectrum beta lactamase (ESBL) producing gram negative organisms, which have often posed therapeutic challenges. All multi drug resistant E.coli, in our study, were ESBL producers and 12 % produced both ESBL and AmpC. 41.66 % of isolated Klebsiella pneumoniae were ESBL producers. 65 % of Proteus mirabilis were ESBL producers (check table 8). 62 out of the 196 gram negative isolates (31.63%) were ESBL producers, which were isolated from 26.59 % of the ulcers in our study. The previous study done at north India[12] showed that 54.5 % of E.coliwere ESBL producers. The other study [72] has showed that 54.6 % of E.coli and 55.8 % of Klebsiella pneumoniae were ESBL producers. The study from Brazil [95] showed 6 % of isolated E.coli were ESBL producers. The study from France [81] has showed 26.9% of Pseudomonas were multi-drug resistant. In our study 4.7 % of isolated organisms were Acinetobacter baumanii and 61.5 % of these were multidrug resistant. In the study from France [81] 25 % of isolated Acenetobacter baumanii were multi-drug resistant.

Among the isolated multi-drug resistant organisms, 25.49 % were MDR E.coli, followed by 22.22 % MDR Pseudomonas aeruginosa, 17.64 % methicillin resistant Staphylococcus aureus. Thus MDROs appear to be firmly entrenched in our patients, and posing questions to clinicians and microbiologists alike, with regard to patient management and the development of antibiotic policies.

In our study, univariate analysis showed that, poor glycaemic control, previous hospitalisation, previous history of amputation, previous antibiotic usage, size of ulcer, necrotic ulcer, recurrent ulcers, higher grade of ulcer, presence of osteomyelitis, presence of retinopathy, peripheral vascular disease, neuropathy and polymicrobial culture, were significantly associated with MDRO infected foot ulcers.

However, analysis by logistic regression revealed that only the recurrent ulcers and higher grade of ulcers were significantly associated with multi-drug resistant organism infections. It is possible that patients with recurrent ulcers have had several courses of antibiotics, both during previous hospital admissions and from practitioners in the community, which led to resistance to multiple antibiotics. Higher grade of ulcers have an associated systemic sepsis and excessive local necrotic tissues.

Another study from India[12] showed that presence of neuropathy and ulcer size > 4 cm^2 were significantly associated with multi-drug resistant organism infections. The two significant factors associated with MDRO, in a study from France [81]were, previous hospitalization and proliferative retinopathy. Previous hospitalisation was again significantly associated in another study from France [60].

Factors like previous hospitalization, previous antibiotic usage, poor glycemic control, ischemic ulcers have emerged as possible risk factors for MDRO in several other studies[12,60,81]. However, we have not found any significant association in our study.

Although we have identified a few factors associated with MDRO, the effect of diabetes related immunopathology has not been studied. This and its possible impact on infection are still a matter of debate [96.]

In our study, the presence of MDRO in foot ulcers, significantly increased the duration of hospital stay and the associated cost. The mean duration of hospital stay in MDRO infected ulcer group was 15.36 days and that of non-MDRO group was 8.8 days. Interestingly, the other two Indian studies (Gadepalli et al [12], Mohammed zubair[72]) found no difference in the duration of hospital stay with MDRO infected ulcers.

Patients with MDRO had an increased the rate of amputations both major and minor, in our study. Similar observations were found in the north Indian study (Mohammedzubair et al [72]) and one from France (Richard et al [81]). We have seen that MDRO infections are associated with higher grade ulcers, and this could offer an explanation for the increased amputations.

We also made an effort to analyse the factors involved in determining the healing time of infected foot ulcers. We found by multi-variate analysis, the factors which determine the wound healing were, the age, presence of peripheral arterial disease, osteomyelitis, nephropathy, interdigital ulcers, poorglycaemic control and grade of ulcer.

Although found significant by univariate analysis, the presence of MDRO had no role in determining the wound healing. This could be because of prompt change of antibiotics as dictated by the culture and sensitivity reports. Similarly other factors like smoking, size and depth of ulcers, duration of diabetes had no role in influencing the duration of wound healing. Similar observations were found in the study from France [81], which also showed no role of MDRO in wound healing. The same study reported that the presence neuro-ischaemic ulcers, proliferative retinopathy, and glycaemic control were the determining factors. Similar reports were observed from other studies (Harteman et al [60], game et al[97]). Wound depth, presence of neuropathy and peripheral arterial disease have been reported to influence wound healing [98,99] . But few studies (Tentolorius et al [50], Wagner et al [100]) have reported that the presence of MRSA, does have a role in prolonging the wound healing time.

CONCLUSION

- The prevalence of multi-drug resistant organisms is alarmingly high in infected diabetic foot ulcers.
- Recurrent ulcers are more prone to acquire multi-drug resistant organisms.
- Higher grade of ulcers are more prone to acquire multi-drug resistant organisms.
- Escherichia coli is commonest isolate from all the ulcers
- ESBL Escherichia coli is the commonest multi-drug resistant organism derived from infected diabetic foot ulcer.
- Multi-drug resistant organisms in diabetic foot ulcers are associated with longer duration of hospital stay.
- Rate of amputations are significantly higher with multi-drug resistant organism infected diabetic foot ulcers.
- Multi-drug resistant organisms have no significant impact on wound healing.
- Presence peripheral arterial disease, osteomyelitis, nephropathy, inter-digital / digital ulcers, higher grade of ulcer and poor glycemic control delay the healing of foot ulcer.
- Prevalence of micro-vascular complications are high in our country.

RECOMMENDATIONS

There is a paucity of data regarding the actual burden of multi-drug resistant organisms in diabetic foot ulcers in our country. The findings from the present study suggest that prospective multicentre studies have to be done to assess the nationwide prevalence and to frame an effective antibiotic policy. The study also directs us to manage the diabetic foot ulcers with appropriate antibiotics adhering to the institutional antibiotic policy along with effective glycemic control to decrease the incidence of multi-drug resistant organisms.

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Ip . no	age	sex	ses	yrs	ulcer	stay	size	depth	na ture	recur	grade	eye	kidney	bone	pvd	nerve	sht	Rx	HE AL	dis	hba1c	hosp	sm oke	alc ohol	ampute	site	antibio	cul ture	mdro
i11004541	52	1	3	1	1	26	5	1	2	0	5	1	1	0	1	1	0	3	5	1	1	0	1	1	0	7	0	1	1
i11013626	63	1	3	1	1	14	4	1	2	0	4	1	0	0	1	1	0	2	2	1	1	1	1	1	0	7	0	2	1
i11013873	62	1	2	3	1	11	3	1	2	1	4	0	0	1	1	1	1	3	5	1	3	1	1	1	0	4	1	2	0
i11016215	25	1	2	2	2	4	3	1	1	0	2	0	0	0	0	0	1	1	1	1	2	0	0	0	0	5	0	2	1
i11023590	49	2	3	2	2	30	3	2	2	1	4	1	1	1	0	1	1	2	3	1	1	1	0	0	0	2	1	2	0
i11029803	64	1	2	3	1	16	4	1	2	1	5	0	0	1	1	1	0	4	6	1	3	1	1	1	0	5	0	2	1
i11034531	58	1	3	2	4	10	3	1	1	1	3	0	0	0	1	1	1	1	2	1	2	1	1	1	0	3	0	1	1
i11003371	71	1	2	2	1	27	2	1	2	0	3	0	1	0	1	1	1	2	2	1	1	1	1	0	1	5	0	1	1
i11003390	60	2	1	1	1	20	2	1	2	0	2	0	0	1	1	1	1	2	3	1	2	0	0	0	0	3	0	2	1
i11000160	60	2	1	1	1	13	2	1	1	0	2	0	0	0	1	0	0	2	2	1	2	1	0	0	0	6	1	1	0
i11019583	60	1	1	2	2	4	1	1	1	1	1	0	0	1	1	1	1	1	2	1	1	1	0	1	1	6	1	2	0
i11033672	69	1	2	2	1	15	2	1	1	1	1	0	0	1	0	1	0	2	3	1	2	1	1	1	1	1	1	2	1
i11016485	75	2	3	3	1	3	2	1	1	0	1	0	1	0	0	1	0	2	2	1	2	1	0	0	0	1	1	1	0
i11028370	57	1	2	1	1	10	4	1	2	0	3	0	0	0	1	1	1	2	3	1	3	0	0	0	0	6	0	2	1
i11035742	49	1	1	2	2	4	3	1	1	0	3	1	1	1	0	0	1	1	2	1	2	1	1	1	0	3	1	2	1
i11013769	50	1	2	3	1	6	1	1	1	0	5	0	0	0	1	1	1	3	5	1	3	1	1	1	0	2	1	1	1
I11013871	59	1	3	2	1	30	4	1	1	1	5	1	0	1	1	1	1	4	6	1	3	1	1	1	0	3	1	2	1
i11035052	52	1	1	3	2	4	2	1	1	1	2	1	0	0	1	0	1	1	2	1	2	1	1	0	0	5	1	2	1
i11004368	38	2	2	1	2	12	3	2	2	1	4	0	0	1	1	1	0	2	3	1	3	1	0	0	0	3	1	2	0
i11012036	64	1	3	1	2	30	5	1	2	1	3	0	0	0	1	1	0	2	3	1	3	1	1	1	0	2	0	1	1
i11013873	62	1	2	3	2	11	2	1	1	0	2	0	0	0	0	0	1	1	2	1	3	0	1	0	0	1	1	1	0
i11014083	58	2	3	2	1	7	3	1	1	1	3	0	0	0	1	1	1	2	3	1	3	1	0	0	0	3	1	2	1
i11017700	67	2	1	1	1	6	3	2	2	0	3	0	1	0	0	1	1	3	5	1	2	1	0	0	0	4	0	1	0
i11017586	45	2	2	1	1	6	3	1	1	0	4	0	0	0	0	1	1	3	5	1	3	0	0	0	1	4	0	1	0
i11017305	76	1	3	3	1	5	2	1	2	0	4	1	1	1	1	1	0	3	5	1	2	1	1	1	0	3	0	2	0
i11016841	56	1	1	3	3	9	1	1	1	1	1	0	0	0	1	1	1	2	1	1	2	1	1	0	0	3	1	1	1
i11016797	55	1	1	3	3	5	3	2	1	1	2	1	1	0	0	1	1	2	2	1	1	1	0	1	1	3	1	1	0
i11016420	57	2	3	2	3	6	3	1	1	1	3	0	1	0	0	1	0	2	2	1	1	0	0	0	0	2	1	1	1
i11016307	55	2	2	1	2	19	4	1	1	0	4	0	0	0	0	1	0	3	5	1	2	0	0	0	1	3	1	2	1
i11006481	70	1	2	2	1	5	2	1	1	0	2	1	0	0	1	0	0	1	3	1	3	1	0	0	0	3	0	2	1

Ip . no	age	sex	ses	yrs	ulcer	stay	size	depth	na ture	recur	grade	eye	kidney	bone	pvd	nerve	sht	Rx	HE AL	dis	hba1c	hosp	sm oke	alc ohol	ampute	site	antibio	cul ture	mdro
i11015847	65	1	1	2	1	10	3	1	2	1	3	1	0	1	1	1	1	4	6	1	3	1	1	0	1	6	1	2	1
i11022480	50	1	2	2	4	14	4	1	2	0	4	0	1	0	1	1	1	3	5	1	2	0	1	0	0	4	1	2	1
i11006024	55	1	3	2	1	25	3	1	2	0	5	0	0	0	1	1	0	4	6	1	3	0	0	0	0	3	0	2	1
i11000493	45	1	2	1	1	2	3	2	2	0	5	0	0	0	0	1	0	3	5	1	3	1	1	0	0	2	1	1	0
i11003875	66	2	3	2	1	5	2	1	1	0	2	0	0	0	0	1	1	1	2	1	2	1	0	1	0	1	0	1	0
i11006760	63	1	4	2	2	7	2	1	2	1	3	0	0	1	1	1	0	2	3	1	2	0	1	0	0	5	0	2	1
i11031011	63	2	3	1	3	20	3	1	2	0	3	0	1	0	1	1	0	2	3	1	3	0	0	0	0	4	0	1	1
i11006024	55	1	3	4	1	25	3	1	2	1	5	1	1	1	1	1	0	4	6	1	3	0	1	1	1	6	0	2	1
i11007987	65	1	4	3	2	10	3	1	1	1	3	0	0	0	1	1	0	2	2	1	2	0	0	0	0	3	0	1	1
i11020303	58	1	3	4	1	60	4	1	2	1	5	1	0	1	1	1	0	4	6	1	3	0	1	0	1	6	0	2	1
i11024587	64	1	2	3	1	7	2	1	2	1	5	1	0	1	0	1	0	4	6	1	3	0	0	1	0	6	0	2	1
i11030786	53	1	2	1	2	3	1	1	1	0	1	0	0	0	0	0	1	1	1	1	1	1	1	0	0	1	0	1	0
i11032172	81	1	3	4	3	7	2	1	2	1	4	0	1	1	1	1	0	3	5	1	2	0	0	0	0	1	1	2	1
i11034824	54	1	1	2	1	4	1	1	2	0	4	1	0	1	1	1	0	3	5	1	3	0	1	0	0	1	0	2	1
i11035695	64	2	3	1	1	25	4	1	2	1	3	0	0	0	1	1	0	2	3	1	3	0	0	0	0	6	1	2	1
i11018186	65	1	1	2	4	7	3	1	1	0	2	0	0	0	0	0	1	1	1	1	2	1	0	0	0	2	0	2	0
i11019213	45	1	4	1	2	6	2	1	1	0	1	0	0	0	0	0	1	1	1	1	1	0	0	0	0	1	0	1	0
i11019046	33	1	3	2	1	8	3	2	2	1	4	0	1	0	1	1	0	2	3	1	3	0	1	0	0	4	1	2	1
i11018282	63	1	2	1	1	3	3	1	2	1	3	0	0	1	1	1	0	3	5	1	2	0	1	1	0	2	0	2	1
i12001780	34	1	2	3	1	6	3	1	1	0	2	0	0	0	0	1	0	2	2	1	3	0	0	1	0	2	1	1	1
i12001726	67	2	4	1	1	6	3	1	1	0	1	0	0	0	0	0	1	1	1	1	1	0	0	0	0	3	0	2	0
i11035695	67	2	3	2	3	23	4	2	1	1	2	0	1	0	0	1	0	3	5	1	3	1	0	0	0	4	0	2	1
i11029803	67	1	2	3	1	16	3	1	2	1	5	1	0	1	1	1	1	4	6	1	3	1	1	1	1	3	1	2	1
i11035303	34	1	2	2	1	28	3	1	2	1	4	1	0	0	1	1	1	4	6	1	2	1	1	0	1	6	1	2	1
i11000153	45	2	3	1	1	29	3	1	1	0	3	0	0	0	1	0	0	3	5	1	1	1	0	0	0	3	0	2	1
i11008790	51	1	2	1	1	9	2	2	2	0	4	0	1	0	1	1	1	4	6	1	3	1	1	1	0	5	0	1	1
i11027474	65	1	2	2	1	10	3	1	2	0	5	0	1	0	1	1	0	4	6	1	3	1	1	0	0	6	1	2	1
i11006760	63	1	3	1	1	7	2	2	2	0	2	0	0	0	0	0	1	1	2	1	1	0	0	0	0	3	0	2	0
i11009665	64	2	3	2	1	4	3	1	1	1	3	0	0	0	1	1	0	1	3	1	3	1	0	0	1	2	0	2	1
i11010406	50	1	2	1	2	3	2	2	1	0	2	0	0	0	0	0	1	1	2	1	1	0	1	0	0	1	0	1	0
i11023590	49	2	1	1	1	41	2	1	2	1	3	0	1	1	0	1	1	2	3	1	2	1	0	0	0	3	0	2	1
i11003319	59	1	2	2	1	43	3	1	2	1	3	0	0	0	1	1	1	2	3	1	3	1	1	0	0	4	0	2	1

Ip . no	age	sex	ses	yrs	ulcer	stay	size	depth	na ture	recur	grade	eye	kidney	bone	pvd	nerve	sht	Rx	HE AL	dis	hba1c	hosp	sm oke	alc ohol	ampute	site	antibio	cul ture	mdro
i11013608	64	1	2	1	1	4	2	2	1	0	4	1	0	1	1	1	0	2	3	1	3	1	0	0	0	2	1	1	1
i11033555	45	1	2	1	2	6	3	1	1	1	2	0	1	0	1	0	1	2	3	1	3	1	1	0	1	6	0	1	1
i11008859	57	1	1	1	2	3	4	1	1	1	2	0	0	0	1	1	1	2	3	1	3	0	1	1	0	1	1	2	1
i11019336	61	1	2	1	3	16	4	2	1	0	2	0	0	0	1	1	1	2	2	1	1	0	1	0	0	2	0	1	0
i11006415	47	1	1	4	1	22	2	1	2	1	3	1	1	0	1	1	0	3	5	1	1	0	1	1	0	1	0	2	1
i10052376	65	1	1	2	1	17	2	2	1	0	1	0	1	0	0	1	1	2	2	1	2	0	0	0	0	1	0	2	0
i11001634	58	1	2	1	2	11	5	1	1	0	2	1	0	0	0	1	0	2	3	1	2	1	0	1	0	4	0	1	1
i11006781	70	1	3	2	1	20	2	1	2	0	3	0	0	0	0	0	0	2	2	1	2	1	1	0	0	3	1	1	1
i11013608	64	1	2	1	1	4	2	1	2	1	3	0	1	0	1	1	0	2	3	1	3	1	1	1	0	3	0	1	1
i11018282	63	1	2	1	1	4	3	2	1	0	1	0	0	0	0	1	1	1	2	1	1	0	0	0	0	5	0	1	0
i11021390	60	1	1	1	1	22	3	2	1	0	2	0	0	0	0	1	1	2	2	1	2	0	0	1	0	6	0	2	0
i11021623	65	1	2	1	1	24	2	1	2	1	3	0	1	0	0	1	0	2	3	1	2	1	0	1	0	1	0	1	1
i11032172	81	1	2	5	1	7	2	1	2	1	4	1	1	1	1	1	1	3	5	1	3	1	1	0	1	3	0	2	1
i11032535	66	1	2	1	1	32	5	1	2	1	4	0	0	0	0	1	1	2	2	1	2	1	1	1	0	4	0	2	1
i11033621	64	2	4	1	1	18	4	1	2	0	3	0	1	0	0	1	1	2	3	1	1	0	0	0	0	5	0	2	1
i11035695	64	2	4	1	1	23	4	1	2	1	3	0	1	0	0	1	0	2	2	1	1	1	0	0	0	5	1	2	1
i11003668	40	2	2	2	1	14	3	2	1	0	2	0	0	0	0	0	0	2	2	1	2	0	0	0	0	4	0	1	0
i11007908	50	1	3	3	1	13	3	2	1	0	2	0	0	0	0	1	0	1	2	1	1	0	1	0	0	3	0	1	0
i11015052	60	1	2	1	1	6	4	2	1	0	2	0	1	0	0	0	0	1	2	1	2	0	0	0	0	2	0	1	0
i11015372	67	1	3	1	1	5	2	2	1	0	2	0	0	0	0	0	0	1	1	1	1	0	0	1	0	2	0	2	0
i11016035	65	1	1	1	1	7	1	2	1	0	1	0	0	0	0	1	1	2	2	1	2	0	1	0	0	3	0	1	0
i11017812	74	1	3	1	1	2	2	2	1	0	2	0	1	0	1	1	0	2	2	1	1	0	0	1	0	6	0	1	0
i11020851	62	1	2	2	3	5	3	2	2	1	3	0	1	0	1	0	1	3	5	1	2	1	1	1	0	3	0	2	0
i11021390	60	1	2	1	1	28	4	2	1	0	2	0	1	1	0	1	1	2	2	1	2	0	1	0	0	5	0	2	0
i11025934	53	1	1	1	1	13	1	2	1	0	1	0	0	0	0	1	1	2	1	1	2	1	0	0	1	1	1	1	0
i11031667	59	1	2	4	4	19	2	1	2	1	4	0	1	1	1	1	1	4	6	1	1	1	0	1	0	2	0	1	1
i11032332	55	1	3	1	1	3	3	2	1	0	2	0	1	1	0	0	0	2	3	1	3	0	1	1	0	3	0	1	0
i11033590	66	1	2	1	1	17	5	1	1	1	3	0	1	0	1	1	1	2	3	1	3	1	0	0	0	4	1	1	1
i11006024	55	1	1	2	1	26	3	1	2	1	5	0	1	1	1	1	1	4	6	1	2	1	1	0	0	6	0	2	1
i11023570	47	1	3	1	1	3	2	1	1	0	2	0	0	0	0	0	0	2	2	1	3	1	1	1	0	3	0	1	1
i11032164	53	1	2	2	1	4	2	1	2	1	2	0	1	1	0	1	1	2	3	1	2	1	1	1	1	2	1	1	1
i11034824	54	1	2	2	2	4	3	1	2	1	3	0	1	1	0	1	1	3	5	1	3	1	1	1	1	2	0	2	1

Ip . no	age	sex	ses	yrs	ulcer	stay	size	depth	na ture	recur	grade	eye	kidney	bone	pvd	nerve	sht	Rx	HE AL	dis	hba1c	hosp	sm oke	alc ohol	ampute	site	antibio	cul ture	mdro
i11003875	66	2	1	2	2	4	1	1	1	0	1	0	0	0	0	1	1	1	1	1	2	0	0	0	0	1	0	2	0
i11017472	58	1	2	1	4	8	2	2	1	1	2	0	1	0	0	0	0	2	4	1	3	1	0	0	0	3	1	2	1
i11020851	62	1	1	2	3	6	3	1	1	0	2	0	1	0	1	1	1	3	5	1	2	0	0	0	0	3	0	2	0
i12005945	55	1	2	1	1	22	3	2	2	1	3	0	1	0	0	1	1	2	3	1	3	1	0	0	0	4	1	2	1
i12024495	57	1	3	1	1	10	4	2	2	1	3	1	1	1	1	1	1	2	3	1	3	1	0	1	0	3	1	2	1
i12021336	60	2	1	4	1	12	2	2	1	0	1	0	1	0	0	0	1	2	1	1	3	0	0	0	0	1	0	1	0
i12014431	61	1	3	3	2	26	2	2	1	1	3	1	0	1	0	1	1	3	5	1	2	0	1	1	1	2	1	2	1
i12012359	53	2	3	1	2	11	4	1	1	0	2	0	0	0	0	1	0	1	1	1	1	0	0	0	0	4	0	1	0
i12000503	70	2	2	5	1	8	3	2	2	0	4	1	1	1	0	1	0	3	5	1	2	1	0	0	0	2	1	1	0
i12002049	45	1	3	2	1	5	2	1	1	0	2	0	1	0	0	0	1	3	5	1	1	0	1	1	0	3	0	1	0
i12002262	64	1	1	1	1	8	3	2	2	1	3	0	0	0	1	1	1	2	2	1	2	1	1	0	1	2	1	1	1
i12002372	52	1	2	2	1	7	1	2	1	0	3	0	1	1	1	1	1	3	5	1	3	1	1	1	1	2	1	2	1
i12002494	52	2	1	2	1	30	2	1	1	0	2	1	1	0	1	1	0	1	2	1	2	1	0	0	1	3	1	1	0
i12002563	56	2	1	2	1	24	4	2	2	1	3	0	1	0	0	1	1	3	5	1	3	1	0	0	0	4	1	2	1
i12016234	62	2	1	3	1	9	2	2	2	0	4	0	1	1	0	1	1	3	5	1	3	0	0	0	0	3	0	2	1
i12019933	58	1	2	1	2	7	2	2	2	1	4	0	1	0	1	1	1	3	5	1	3	0	0	0	0	4	0	2	1
i12019108	61	1	2	3	2	10	3	2	1	0	1	1	1	0	0	1	0	1	1	1	2	0	1	0	0	3	0	2	0
i12019933	58	1	3	1	1	16	3	2	2	1	4	0	1	1	1	1	1	3	5	1	3	1	1	1	1	2	1	2	1
i12000124	65	1	2	2	1	14	2	2	1	0	3	0	1	0	0	1	1	2	3	1	3	0	1	1	0	5	0	2	1
i12001174	52	1	1	3	1	10	3	2	1	1	3	0	1	0	0	0	0	2	2	1	3	1	1	1	1	5	1	1	1
i12009073	73	1	1	3	2	5	2	2	2	1	4	1	0	1	1	1	1	3	5	1	3	1	1	1	0	3	1	2	1
i12012893	51	2	3	2	2	8	3	2	2	0	4	0	0	1	0	1	0	3	5	1	3	1	0	0	1	4	1	2	1
i12021402	65	2	2	1	1	22	2	2	1	0	3	0	0	0	0	0	0	2	2	1	2	0	0	0	0	5	0	1	1
i12012893	51	2	2	2	1	9	3	2	2	0	4	0	0	0	0	1	1	3	5	1	3	0	0	0	0	4	1	2	1
i12002563	56	2	3	1	1	4	2	1	1	1	2	0	0	0	0	0	0	2	1	1	2	0	0	0	0	5	0	2	0
i12013972	54	2	2	1	1	8	3	2	1	0	3	0	1	0	0	1	1	2	2	1	2	0	0	0	0	5	0	1	0
i12016234	62	2	3	2	1	16	4	1	1	0	3	0	1	1	0	1	1	3	5	1	3	1	0	0	0	4	1	2	1
i12018932	34	1	2	2	1	8	3	1	1	0	2	0	0	0	1	0	0	3	5	1	2	0	1	1	0	4	0	2	0
i12019108	61	1	2	3	2	4	2	1	1	0	2	1	1	0	0	1	1	3	5	1	3	0	1	1	0	4	0	2	0
i12023468	48	1	2	3	1	8	3	1	1	0	2	0	1	0	0	0	1	1	1	1	1	0	1	1	0	4	0	2	0
i12000995	60	1	3	1	1	15	5	2	2	0	4	0	1	1	0	1	1	1	3	1	3	0	1	0	0	4	1	1	1
i12017012	66	2	2	3	1	12	4	2	2	1	4	0	1	1	0	1	1	3	5	1	3	1	0	0	0	4	1	1	1

Ip . no	age	sex	ses	yrs	ulcer	stay	size	depth	na ture	recur	grade	eye	kidney	bone	pvd	nerve	sht	Rx	HE AL	dis	hba1c	hosp	sm oke	alc ohol	ampute	site	antibio	cul ture	mdro
i12014705	58	1	2	2	1	5	3	1	1	1	2	0	0	0	1	1	1	2	3	1	3	0	1	1	0	4	0	1	0
i12002262	64	1	2	3	2	8	2	1	1	0	1	0	1	0	0	1	1	1	2	1	3	0	1	1	0	5	0	1	0
i12012893	51	2	2	3	1	15	3	2	2	1	4	1	1	1	0	1	0	3	5	1	3	1	0	0	0	4	1	2	1
i11034824	54	1	3	2	1	32	4	2	2	1	4	0	1	1	1	1	1	3	5	1	3	1	0	1	1	3	1	2	1
i12020408	61	1	2	3	1	12	3	2	1	1	2	0	0	1	0	1	1	1	2	1	2	1	1	1	1	2	1	2	1
i12007346	55	1	1	3	1	17	4	2	2	1	5	1	1	1	1	1	1	4	6	1	3	1	1	1	0	6	1	1	1
i12012152	55	2	1	4	2	28	3	2	1	0	4	0	0	1	0	1	0	3	5	1	3	1	0	0	1	4	1	2	1
i11034824	54	1	2	2	1	40	3	1	2	1	3	0	0	0	0	0	1	2	2	1	2	1	0	0	1	5	1	2	1
i11036295	65	2	1	1	1	30	2	2	2	0	4	0	1	0	0	1	1	2	2	1	2	0	0	0	0	3	0	2	1
i12001458	66	1	1	4	2	12	3	1	2	0	4	0	1	0	0	1	1	3	5	1	1	1	1	1	0	3	0	2	1
i12005065	47	1	2	2	2	5	2	1	1	1	2	0	1	0	1	1	1	1	2	1	2	1	1	1	1	2	1	1	0
i12009073	73	1	1	1	2	13	3	2	2	1	4	1	1	0	1	1	1	1	2	1	3	0	1	1	0	3	0	2	1
i12012153	64	1	1	4	2	13	2	1	1	1	2	1	1	1	0	1	1	1	2	1	2	1	0	1	1	3	1	2	1
i12014431	61	1	2	2	1	26	3	1	2	0	3	1	1	1	0	1	1	2	2	1	1	1	0	1	0	4	1	2	1
i21015232	49	1	1	2	2	3	2	1	1	0	1	0	0	0	0	0	0	1	2	1	3	0	1	1	0	4	0	1	0
i12000995	60	1	1	2	1	6	3	1	2	1	3	0	1	1	1	1	1	2	3	1	2	1	1	1	0	3	1	1	1
i12002823	64	1	2	2	1	8	3	2	2	1	4	1	1	0	0	1	1	3	5	1	3	1	0	0	1	4	1	1	1
i12003160	35	1	1	1	1	9	3	1	1	0	3	0	0	0	1	0	1	2	3	1	3	0	1	0	0	6	0	2	1
i12006343	61	1	3	1	1	21	2	1	1	1	3	1	1	0	1	0	1	2	2	1	1	0	1	1	0	3	1	2	1
i12009179	63	1	2	2	1	14	1	1	1	0	1	0	0	0	0	0	0	1	1	1	1	1	0	0	0	3	0	1	0
i12005018	63	1	2	1	2	23	2	2	2	0	4	1	1	1	1	1	1	3	5	1	3	0	1	1	0	4	0	2	1
i12006648	53	1	1	1	1	8	4	1	2	1	3	1	0	1	0	1	1	2	3	1	2	0	1	0	0	4	0	2	1
i12008244	75	1	2	4	1	4	1	2	2	1	3	0	0	1	1	1	1	2	3	1	2	0	0	1	0	2	0	1	1
i12011769	59	1	1	4	1	13	3	2	1	1	4	1	1	1	1	1	1	3	5	1	3	0	1	1	1	5	1	1	1